

[File Copy]

10/813,647

=> d his

(FILE 'HOME' ENTERED AT 11:04:52 ON 02 OCT 2006)

FILE 'HCAPLUS' ENTERED AT 11:05:11 ON 02 OCT 2006

E US20040266824/PN

L1 1 S US20040266824/PN  
SEL RN

FILE 'REGISTRY' ENTERED AT 11:06:30 ON 02 OCT 2006

L2 67 S E1-E67

FILE 'LREGISTRY' ENTERED AT 11:07:28 ON 02 OCT 2006

L3 STR

FILE 'REGISTRY' ENTERED AT 11:16:36 ON 02 OCT 2006

L4 0 S L3

FILE 'LREGISTRY' ENTERED AT 11:23:30 ON 02 OCT 2006

L5 STR L3

FILE 'REGISTRY' ENTERED AT 11:24:39 ON 02 OCT 2006

L6 SCR 1838

L7 SCR 1918 OR 2043 OR 1843

L8 0 S L5 AND L6 NOT L7

L9 SCR 1100

L10 SCR 1992

L11 1 S L5 AND L6 AND L9 AND L10 NOT L7

L12 SCR 1918 OR 2043

L13 1 S L5 AND L6 AND L9 AND L10 NOT L12

L14 451 S L5 AND L6 AND L9 AND L10 NOT L12 FUL

SAV L14 DAV647/A

L15 16 S L2 AND L14

FILE 'HCAPLUS' ENTERED AT 11:37:49 ON 02 OCT 2006

L16 812 S L15

L17 969 S L14

L18 QUE PHARMAC?/SC,SX

L19 598 S L16 AND L18

L20 703 S L17 AND L18

FILE 'LREGISTRY' ENTERED AT 11:40:03 ON 02 OCT 2006

L21 STR L5

FILE 'REGISTRY' ENTERED AT 11:46:21 ON 02 OCT 2006

L22 24 S L21 SSS SAM SUB=L14

L23 451 S L21 SSS FUL SUB=L14

L24 306 S L23 NOT 6-20/NR

FILE 'HCAPLUS' ENTERED AT 11:51:49 ON 02 OCT 2006

L25 965 S L24

L26 617 S L20 AND 1907-1999/PY,PRY

E CNS/CT

L27 QUE CNS OR CENTRAL(3N)NERVOUS(3N)(SYS OR SYSTEM)

L28 26 S L26 AND L27

FILE 'LREGISTRY' ENTERED AT 12:02:39 ON 02 OCT 2006

L29 STR L21

FILE 'REGISTRY' ENTERED AT 12:07:55 ON 02 OCT 2006

L30 23 S L29 SSS SAM SUB=L14

L31 184 S L24 AND 1/NC

L32 122 S L24 NOT L31

FILE 'HCAPLUS' ENTERED AT 12:11:14 ON 02 OCT 2006

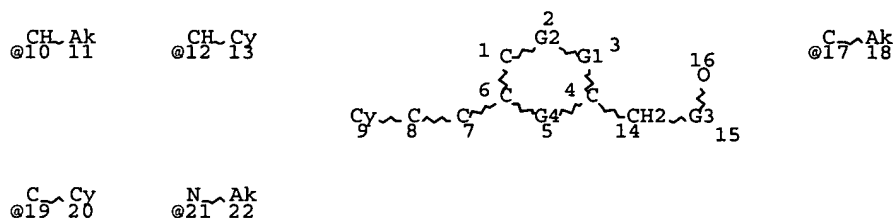
L33 846 S L31

10/813,647

L34 169 S L32  
 L35 88 S L14/THU  
 L36 33 S L35 AND L26  
 L37 53 S L36 OR L28  
 L38 QUE (DRUG? OR NARCOT?) (2N) (ABUSE# OR ABUSING OR ADDICT?  
 E ANOREXIA/CT  
 E E3+ALL  
 L39 1540 S ANOREXIA/CT  
 E BULIMIA/CT  
 E E3+ALL  
 L40 672 S BULIMIA/CT  
 L41 QUE EAT? (2N) (DISORDER? OR DISEASE) OR L39 OR L40  
 L42 3 S L26 AND L41  
 L43 1 S L26 AND (ANOREXIA? OR BULIMIA?)  
 L44 53 S L37 OR L42 OR L43

=> d que stat

L5 STR



REP G1=(0-4) C  
 VAR G2=CH2/10/12  
 VAR G3=CH/17/19  
 VAR G4=NH/21  
 NODE ATTRIBUTES:  
 CONNECT IS E1 RC AT 16  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED  
 GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L6 SCR 1838  
 L9 SCR 1100  
 L10 SCR 1992  
 L12 SCR 1918 OR 2043  
 L14 451 SEA FILE=REGISTRY SSS FUL L5 AND L6 AND L9 AND L10 NOT  
 L12  
 L17 969 SEA FILE=HCAPLUS ABB=ON PLU=ON L14  
 L18 QUE ABB=ON PLU=ON PHARMAC?/SC,SX  
 L20 703 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L18  
 L26 617 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND 1907-1999/PY,P  
 RY  
 L27 QUE ABB=ON PLU=ON CNS OR CENTRAL(3A)NERVOUS(3A)(SYS  
 OR SYSTEM)  
 L28 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND L27  
 L35 88 SEA FILE=HCAPLUS ABB=ON PLU=ON L14/THU  
 L36 33 SEA FILE=HCAPLUS ABB=ON PLU=ON L35 AND L26  
 L37 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L36 OR L28  
 L39 1540 SEA FILE=HCAPLUS ABB=ON PLU=ON ANOREXIA/CT  
 L40 672 SEA FILE=HCAPLUS ABB=ON PLU=ON BULIMIA/CT  
 L41 QUE ABB=ON PLU=ON EAT? (2A) (DISORDER? OR DISEASE) OR  
 L39 OR L40  
 L42 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND L41

10/813,647

L43 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND (ANOREXIA? OR  
BULIMIA?)  
L44 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L37 OR L42 OR L43

=>

=&gt; d his ful

(FILE 'HOME' ENTERED AT 11:04:52 ON 02 OCT 2006)

FILE 'HCAPLUS' ENTERED AT 11:05:11 ON 02 OCT 2006

E US20040266824/PN

L1 1 SEA ABB=ON PLU=ON US20040266824/PN  
D ALL  
SEL RN

FILE 'REGISTRY' ENTERED AT 11:06:30 ON 02 OCT 2006

L2 67 SEA ABB=ON PLU=ON (108-48-5/BI OR 134-64-5/BI OR  
324078-19-5/BI OR 324078-32-2/BI OR 324078-36-6/BI OR  
324078-40-2/BI OR 324078-41-3/BI OR 324078-52-6/BI OR  
3277-89-2/BI OR 530-51-8/BI OR 552-72-7/BI OR 579-21-5/  
BI OR 620-08-6/BI OR 650636-96-7/BI OR 6738-06-3/BI OR  
748756-00-5/BI OR 752188-91-3/BI OR 758717-83-8/BI OR  
758717-85-0/BI OR 758717-86-1/BI OR 818377-08-1/BI OR  
818377-09-2/BI OR 818377-10-5/BI OR 818377-11-6/BI OR  
818377-12-7/BI OR 818377-13-8/BI OR 818377-14-9/BI OR  
818377-15-0/BI OR 818377-16-1/BI OR 818377-17-2/BI OR  
818377-18-3/BI OR 818377-19-4/BI OR 818377-20-7/BI OR  
818377-21-8/BI OR 818377-22-9/BI OR 818377-23-0/BI OR  
818377-24-1/BI OR 818377-25-2/BI OR 818377-26-3/BI OR  
818377-27-4/BI OR 818377-28-5/BI OR 818377-29-6/BI OR  
818377-30-9/BI OR 818377-31-0/BI OR 818377-32-1/BI OR  
818377-33-2/BI OR 818377-34-3/BI OR 818377-35-4/BI OR  
818377-36-5/BI OR 818377-37-6/BI OR 818377-38-7/BI OR  
818377-39-8/BI OR 818377-40-1/BI OR 818377-41-2/BI OR  
818377-42-3/BI OR 818377-43-4/BI OR 818377-44-5/BI OR  
818377-45-6/BI OR 818377-46-7/BI OR 818377-47-8/BI OR  
818377-48-9/BI OR 818377-49-0/BI OR 818377-50-3/BI OR  
818377-51-4/BI OR 818377-52-5/BI OR 818377-53-6/BI OR  
90-69-7/BI)  
D SCAN

FILE 'LREGISTRY' ENTERED AT 11:07:28 ON 02 OCT 2006

L3 STR

FILE 'REGISTRY' ENTERED AT 11:16:36 ON 02 OCT 2006

L4 0 SEA SSS SAM L3

FILE 'LREGISTRY' ENTERED AT 11:23:30 ON 02 OCT 2006

L5 STR L3

FILE 'REGISTRY' ENTERED AT 11:24:39 ON 02 OCT 2006

L6 SCR 1838  
L7 SCR 1918 OR 2043 OR 1843  
L8 0 SEA SSS SAM L5 AND L6 NOT L7  
L9 SCR 1100  
L10 SCR 1992  
L11 1 SEA SSS SAM L5 AND L6 AND L9 AND L10 NOT L7  
D SCAN  
L12 SCR 1918 OR 2043  
L13 1 SEA SSS SAM L5 AND L6 AND L9 AND L10 NOT L12  
D QUE STAT  
L14 451 SEA SSS FUL L5 AND L6 AND L9 AND L10 NOT L12  
SAV L14 DAV647/A  
D SAV  
L15 16 SEA ABB=ON PLU=ON L2 AND L14  
D SCAN

FILE 'HCAPLUS' ENTERED AT 11:37:49 ON 02 OCT 2006

L16 812 SEA ABB=ON PLU=ON L15  
L17 969 SEA ABB=ON PLU=ON L14  
L18 QUE ABB=ON PLU=ON PHARMAC?/SC,SX

10/813,647

L19 598 SEA ABB=ON PLU=ON L16 AND L18  
L20 703 SEA ABB=ON PLU=ON L17 AND L18

FILE 'LREGISTRY' ENTERED AT 11:40:03 ON 02 OCT 2006  
D QUE STAT  
L21 STR L5

FILE 'REGISTRY' ENTERED AT 11:46:21 ON 02 OCT 2006  
L22 24 SEA SUB=L14 SSS SAM L21  
D SCAN  
D QUE STAT  
L23 451 SEA SUB=L14 SSS FUL L21  
L24 306 SEA ABB=ON PLU=ON L23 NOT 6-20/NR

FILE 'HCAPLUS' ENTERED AT 11:51:49 ON 02 OCT 2006  
L25 965 SEA ABB=ON PLU=ON L24  
L26 617 SEA ABB=ON PLU=ON L20 AND 1907-1999/PY, PRY  
L27 QUE ABB=ON PLU=ON CNS OR CENTRAL(3A)NERVOUS(3A) (SYS  
OR SYSTEM)  
L28 26 SEA ABB=ON PLU=ON L26 AND L27  
D QUE STAT

FILE 'LREGISTRY' ENTERED AT 12:02:39 ON 02 OCT 2006  
L29 STR L21

FILE 'REGISTRY' ENTERED AT 12:07:55 ON 02 OCT 2006  
L30 23 SEA SUB=L14 SSS SAM L29  
L31 184 SEA ABB=ON PLU=ON L24 AND 1/NC  
L32 122 SEA ABB=ON PLU=ON L24 NOT L31

FILE 'HCAPLUS' ENTERED AT 12:11:14 ON 02 OCT 2006  
L33 846 SEA ABB=ON PLU=ON L31  
L34 169 SEA ABB=ON PLU=ON L32  
L35 88 SEA ABB=ON PLU=ON L14/THU  
L36 33 SEA ABB=ON PLU=ON L35 AND L26  
L37 53 SEA ABB=ON PLU=ON L36 OR L28  
L38 QUE ABB=ON PLU=ON (DRUG? OR NARCOT?) (2A) (ABUSE# OR  
ABUSING OR ADDICT? OR TREAT?)  
E ANOREXIA/CT  
E E3+ALL  
L39 1540 SEA ABB=ON PLU=ON ANOREXIA/CT  
E BULIMIA/CT  
E E3+ALL  
L40 672 SEA ABB=ON PLU=ON BULIMIA/CT  
L41 QUE ABB=ON PLU=ON EAT?(2A) (DISORDER? OR DISEASE) OR  
L39 OR L40  
L42 3 SEA ABB=ON PLU=ON L26 AND L41  
D SCAN  
L43 1 SEA ABB=ON PLU=ON L26 AND (ANOREXIA? OR BULIMIA?)  
D SCAN  
L44 53 SEA ABB=ON PLU=ON L37 OR L42 OR L43  
D QUE STAT

FILE 'LREGISTRY' ENTERED AT 12:52:31 ON 02 OCT 2006  
L45 STR L29

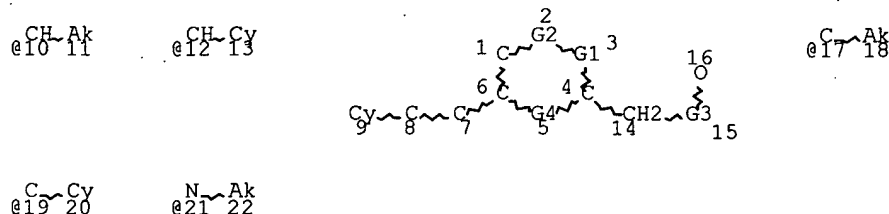
FILE 'REGISTRY' ENTERED AT 12:55:45 ON 02 OCT 2006  
L46 10 SEA SUB=L14 SSS SAM L45  
L47 171 SEA SUB=L14 SSS FUL L45  
SAV L47 DAV647A/A

FILE 'HCAPLUS' ENTERED AT 12:59:04 ON 02 OCT 2006  
L48 959 SEA ABB=ON PLU=ON L47  
L49 82 SEA ABB=ON PLU=ON L47/THU  
L50 80 SEA ABB=ON PLU=ON L49 AND (L18 OR L27 OR L38 OR L41)  
L51 29 SEA ABB=ON PLU=ON L50 AND 1907-1999/PY, PRY

10/813,647

L52 54 SEA ABB=ON PLU=ON L51 OR L44  
L53 25 SEA ABB=ON PLU=ON L44 NOT L51

=> => d que stat 151  
L5 STR

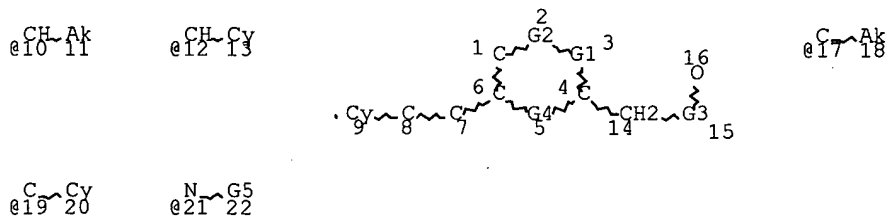


REP G1=(0-4) C  
VAR G2=CH2/10/12  
VAR G3=CH/17/19  
VAR G4=NH/21  
NODE ATTRIBUTES:  
CONNECT IS E1 RC AT 16  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L6 SCR 1838  
L9 SCR 1100  
L10 SCR 1992  
L12 SCR 1918 OR 2043  
L14 451 SEA FILE=REGISTRY SSS FUL L5 AND L6 AND L9 AND L10 NOT L12  
L18 QUE ABB=ON PLU=ON PHARMAC?/SC, SX  
L27 QUE ABB=ON PLU=ON CNS OR CENTRAL(3A) NERVOUS(3A) (SYS OR SYSTEM)  
L38 QUE ABB=ON PLU=ON (DRUG? OR NARCOT?) (2A) (ABUSE# OR A Busing OR ADDICT? OR TREAT?)  
L39 1540 SEA FILE=HCAPLUS ABB=ON PLU=ON ANOREXIA/CT  
L40 672 SEA FILE=HCAPLUS ABB=ON PLU=ON BULIMIA/CT  
L41 QUE ABB=ON PLU=ON EAT?(2A) (DISORDER? OR DISEASE) OR L39 OR L40  
L45 STR



REP G1=(0-4) C  
VAR G2=CH2/10/12  
VAR G3=CH/17/19  
VAR G4=NH/21  
VAR G5=ME/ET/N-PR/I-PR

## NODE ATTRIBUTES:

CONNECT IS E1 RC AT 16  
 DEFAULT MLEVEL IS ATOM  
 GGCAT IS UNS AT 9  
 GGCAT IS UNS AT 13  
 GGCAT IS UNS AT 20  
 DEFAULT ECLEVEL IS LIMITED  
 ECOUNT IS M5-X6 C AT 9  
 ECOUNT IS M1-X4 C AT 11  
 ECOUNT IS M5-X6 C AT 13  
 ECOUNT IS M1-X4 C AT 18  
 ECOUNT IS M5-X6 C AT 20

## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 22

## STEREO ATTRIBUTES: NONE

L47 171 SEA FILE=REGISTRY SUB=L14 SSS FUL L45  
 L49 82 SEA FILE=HCAPLUS ABB=ON PLU=ON L47/THU  
 L50 80 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND (L18 OR L27  
 OR L38 OR L41)  
 L51 29 SEA FILE=HCAPLUS ABB=ON PLU=ON L50 AND 1907-1999/PY,P  
 RY

=> d l51 1-29 ibib abs hitstr hitind

L51 ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:666025 HCAPLUS Full-text  
 DOCUMENT NUMBER: 145:152690  
 TITLE: Method for inducing crystalline state  
 transition in pharmaceuticals  
 INVENTOR(S): Nakamichi, Kouichi; Izumi, Shougo; Oka,  
 Masaaki  
 PATENT ASSIGNEE(S): Nippon Shinyaju Company, Ltd., Japan  
 SOURCE: U.S., 18 pp., Cont.-in-part of U. S.  
 5,456,923.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811547	A	19980922	US 1995-416815	1995 0609
CA 2147279	AA	19940428	CA 1993-2147279	1993 1013
WO 9408561	A1	19940428	WO 1993-JP1469	1993 1013
W: AU, BR, CA, FI, HU, JP, KR, NO, NZ, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9351607	A1	19940509	AU 1993-51607	1993 1013
EP 665009	A1	19950802	EP 1993-922625	

1993  
1013

&lt;--

EP 665009 B1 20000216  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,  
 NL, PT, SE  
 AT 189770 E 20000315 AT 1993-922625

1993  
1013

&lt;--

ES 2145063 T3 20000701 ES 1993-922625

1993  
1013

&lt;--

US 5456923 A 19951010 US 1993-129133

1993  
1115

PRIORITY APPLN. INFO.:

&lt;--

JP 1992-303085 A

1992  
1014

&lt;--

WO 1993-JP1469 W

1993  
1013

&lt;--

US 1993-129133 A2

1993  
1115

&lt;--

JP 1991-112554 A

1991  
0416

&lt;--

WO 1992-JP470 W

1992  
0414

&lt;--

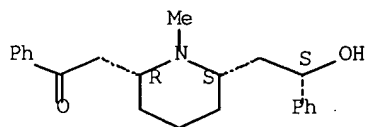
AB This invention has for its object to provide a method of inducing a transition in crystalline state of a crystallizable pharmaceutical with great ease and improved efficiency and uniformity on a high production scale. An extruder is used for inducing a transition from one crystalline state ( $\Delta$ ) to another crystalline state in a crystallizable pharmaceutical. An extruded indomethacin (form  $\alpha$ ) was converted to an amorphous form.

IT 134-63-4, Lobeline hydrochloride  
 RL: PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (method for inducing crystalline state transition in  
 pharmaceuticals)

RN 134-63-4 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidiny]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl



IC ICM C07D209-32  
ICS C07D223-24  
INCL 540589000; 548500000; 564045000; 564213000  
CC 63-6 (Pharmaceuticals)  
IT Allergy inhibitors  
Analgesics  
Anesthetics  
Anthelmintics  
Antiarrhythmics  
Antibiotics  
Anticoagulants  
Anticonvulsants  
Antidiabetic agents  
Antidiarrheals  
Antihypertensives  
Antimicrobial agents  
Antiparkinsonian agents  
Antipyretics  
Antitumor agents  
Antitussives  
Antiviral agents  
Bronchodilators  
Cardiotonics  
Cardiovascular agents  
Central nervous system agents  
Choleretics  
Diuretics  
Expectorants  
Gastrointestinal agents  
Hemostatics  
Laxatives  
Liver, disease  
Narcotics  
Nervous system stimulants  
Polymorphism (crystal)  
Psychotropics  
Structural phase transition  
Tuberculostatics  
Urinary system  
Vasoconstrictors  
Vasodilators  
(method for inducing crystalline state transition in pharmaceuticals)

IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone acetate  
50-04-4, Cortisone acetate 50-06-6, Phenobarbital, biological studies 50-11-3, Metharbital 50-14-6, Ergocalciferol  
50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-27-1, Estriol 50-33-9, Phenylbutazone, biological studies 50-34-0, Propantheline bromide 50-41-9, Clomifene citrate 50-44-2, Mercaptopurine 50-50-0, Estradiol benzoate 50-53-3, biological studies 50-54-4, Quinidine sulfate 50-55-5, Reserpine 50-59-9, Cefaloridine 50-78-2, Aspirin 50-81-7, Ascorbic acid, biological studies 50-98-6, Ephedrine hydrochloride 51-05-8, Procaine hydrochloride 51-21-8, Fluorouracil 51-30-9, Isoprenaline hydrochloride 51-41-2, Norepinephrine 51-43-4, Epinephrine 51-52-5, Propylthiouracil 51-57-0, Methamphetamine hydrochloride 51-77-4, Gefarnate 52-01-7, Spironolactone 52-21-1, Prednisolone acetate 52-24-4, Thiotepa 52-26-6, Morphine hydrochloride 52-28-8, Codeine phosphate 52-49-3, Trihexyphenidyl hydrochloride 52-67-5, Penicillamine 52-86-8, Haloperidol 52-90-4, L-Cysteine, biological studies 53-19-0, Mitotane 53-21-4, Cocaine hydrochloride 53-36-1, Methylprednisolone acetate 53-86-1, Indomethacin 54-21-7, Sodium salicylate 54-31-9, Furosemide 54-36-4, Metyrapone 54-47-7, Pyridoxal phosphate 54-85-3, Isoniazide 55-03-8,

Levothyroxine sodium 55-06-1, Liothyronine sodium 55-31-2,  
 Epinephrine hydrochloride 55-48-1, Atropine sulfate 55-97-0,  
 Hexamethonium bromide 55-98-1, Busulfan 56-29-1, Hexobarbital  
 56-75-7, Chloramphenicol 56-85-9, L-Glutamine, biological  
 studies 57-43-2, Amobarbital 57-44-3, Barbitol 57-63-6,  
 Ethynylestradiol 57-66-9, Probenecid 57-83-0, Progesterone,  
 biological studies 57-85-2, Testosterone propionate 57-94-3,  
 Tubocurarine chloride 57-96-5, Sulfapyrazone 58-18-4,  
 Methyltestosterone 58-25-3, Chlorodiazepoxide 58-28-6,  
 Desipramine hydrochloride 58-32-2, Dipyridamole 58-33-3,  
 Promethazine hydrochloride 58-38-8 58-39-9, Perphenazine  
 58-54-8, Etacrynic acid 58-55-9, Theophylline, biological  
 studies 58-56-0, Pyridoxine hydrochloride 58-71-9 58-73-1D,  
 Diphenhydramine, tannates 58-85-5, Biotin 58-93-5,  
 Hydrochlorothiazide 58-95-7, Tocopherol acetate 59-05-2,  
 Methotrexate 59-30-3, Folic acid, biological studies 59-58-5,  
 Prosultiamine 59-66-5, Acetazolamide 59-67-6, Nicotinic acid,  
 biological studies 59-92-7, Levodopa, biological studies  
 59-97-2, Tolazoline hydrochloride 59-99-4, Neostigmine  
 60-02-6, Guanethidine sulfate 60-31-1, Acetylcholine chloride  
 60-54-8, Tetracycline 60-56-0, Thiamazole 60-99-1,  
 Levomepromazine 61-12-1, Dibucaine hydrochloride 61-16-5,  
 Methoxamine hydrochloride 61-25-6, Papaverine hydrochloride  
 61-56-3, Sultiamine 61-68-7, Mefenamic acid 61-76-7,  
 Phenylephrine hydrochloride 62-31-7, Dopamine hydrochloride  
 62-33-9, Calcium disodium edetate 62-44-2, Phenacetin 62-90-8,  
 Nandrolone phenylpropionate 64-31-3, Morphine sulfate 64-65-3,  
 Bemegride 64-73-3, Demethylchlorotetracycline hydrochloride  
 64-75-5, Tetracycline hydrochloride 64-77-7, Tolbutamide  
 64-86-8, Colchicine 65-28-1, Phentolamine mesylate 65-45-2,  
 Salicylamide 67-03-8, Thiamine hydrochloride 67-16-3, Thiamine  
 disulfide 67-78-7, Triamcinolone diacetate 67-92-5,  
 Dicycloverin hydrochloride 67-96-9, Dihydrotachysterol  
 68-19-9, Cyanocobalamin 68-22-4, Norethisterone 68-41-7,  
 Cycloserine 68-89-3, Sulpyrine 68-91-7, Trimetaphan camsilate  
 69-23-8, Fluphenazine 69-53-4, Ampicillin 69-81-8,  
 Carbazochrome 70-18-8, Glutathione, biological studies  
 71-27-2, Suxamethonium chloride 71-58-9, Medroxyprogesterone  
 acetate 71-63-6, Digitoxin 71-73-8, Thiopental sodium  
 71-78-3, Pipradrol hydrochloride 71-82-9, Levallorphan tartrate  
 72-33-3, Mestranol 73-49-4, Quinethazone 73-78-9, Lidocaine  
 hydrochloride 76-25-5, Triamcinolone acetonide 76-43-7,  
 Fluoxymesterone 76-74-4, Pentobarbital 76-90-4, Mepenzolate  
 bromide 77-36-1, Chlorothalidone 77-67-8, Ethosuximide  
 78-11-5, Pentaerythrityl tetranitrate 79-64-1, Dimethisterone  
 79-81-2, Retinol palmitate 80-08-0, Diaphenyl sulfone 80-50-2,  
 Anisotropine methobromide 80-77-3, Chlormezanone 80-92-2,  
 Pregnanediol 81-23-2, Dehydrocholic acid 83-43-2,  
 Methylprednisolone 83-88-5, Riboflavin, biological studies  
 84-22-0, Tetryzoline 84-36-6, Syrosingopine 84-80-0,  
 Phytonadione 86-35-1, Ethotoin 86-74-8, Chlorophenesin  
 carbamate 87-33-2, Isosorbide dinitrate 90-22-2, Valethamate  
 bromide 90-33-5, Hymecromone 93-14-1, Guaifenesin 94-09-7,  
 Ethyl aminobenzoate 94-20-2, Chloropropamide 94-63-3,  
 Pralidoxime iodide 95-25-0, Chlorzoxazone 97-18-7, Bithionol  
 98-92-0, Nicotinamide 98-96-4, Pyrazinamide 99-26-3, Bismuth  
 subgallate 100-97-0, Hexamine, biological studies 101-26-8,  
 Pyridostigmine bromide 103-90-2, Acetaminophen 107-35-7,  
 2-Aminoethanesulfonic acid 113-07-5, Doxapram hydrochloride  
 113-38-2, Estradiol dipropionate 113-52-0, Imipramine  
 hydrochloride 113-59-7, Chlorprothixene 113-92-8 113-98-4,  
 Benzylpenicillin potassium 114-49-8, Scopolamine hydrobromide  
 114-85-2, Betanidine sulfate 115-79-7, Ambenonium chloride  
 119-41-5, Efloxate 119-48-2, Dimorpholamine 122-11-2,  
 Sulfadimethoxine 124-94-7, Triamcinolone 125-02-0,  
 Prednisolone sodium phosphate 125-04-2, Hydrocortisone sodium  
 succinate 125-30-4, Ethylmorphine hydrochloride 125-33-7,

Primidone 125-52-0, Oxyphencyclimine hydrochloride 126-07-8,  
 Griseofulvin 126-27-2, Oxethazaine 127-07-1, Hydroxycarbamide  
 127-47-9 127-48-0, Trimethadione 127-69-5, Sulfisoxazole  
 128-13-2, Ursodesoxycholic acid 128-62-1, Noscapine 129-51-1,  
 Ergometrine Maleate 129-77-1, Piperidolate hydrochloride  
 130-40-5, Riboflavin sodium phosphate 130-61-0, Thioridazine  
 hydrochloride 132-18-3, Diphenylpyraline teoclate 132-69-4,  
 Benzydamine hydrochloride 132-93-4, Pheneticillin potassium  
 132-98-9, Phenoxymethylpenicillin potassium 133-67-5,  
 Trichloromethiazide 134-63-4, Lobeline hydrochloride  
 135-07-9 135-09-1, Hydroflumethiazide 136-47-0, Tetracaine  
 hydrochloride 138-14-7, Deferoxamine mesylate 142-47-2, Sodium  
 glutamate 144-82-1, Sulfamethizole 146-22-5, Nitrazepam  
 147-24-0, Asdrin 147-94-4, Cytarabine 148-82-3, Melphalan  
 149-64-4, Butylscopolamine bromide 151-73-5, Betamethasone  
 sodium phosphate 152-11-4, Verapamil hydrochloride 152-47-6,  
 Sulfamethopyrazine 152-62-5, Dydrogesterone 153-00-4,  
 Metenolone 153-87-7, Oxypertine 154-23-4, Cianidanol  
 154-87-0, Cocarboxylase 298-46-4, Carbamazepine 298-59-9,  
 Methyl phenidate hydrochloride 299-39-8, Sparteine sulfate  
 299-95-6, Isoproterenol sulfate 302-22-7 302-70-5, Nitrogen  
 mustard N-oxide hydrochloride 303-98-0, Ubidecarenone  
 304-20-1, Hydralazine hydrochloride 309-43-3, Secobarbital  
 sodium 315-30-0, Allopurinol  
 RL: PRP (Properties); **THU (Therapeutic use)**; BIOL  
 (Biological study); USES (Uses)

(method for inducing crystalline state transition in  
 pharmaceuticals)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L51 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:425892 · HCAPLUS Full-text  
 DOCUMENT NUMBER: 144:474902  
 TITLE: Apomorphine for the treatment of organic  
 erectile dysfunction in males  
 INVENTOR(S): Ruff, Dustin D.; Perdok, Renee J.; Kling,  
 Karen  
 PATENT ASSIGNEE(S): Abbott Laboratories, USA  
 SOURCE: Aust. Pat. Appl., 22 pp.  
 CODEN: AUXXCM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

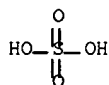
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2005201509	A1	20050505	AU 2005-201509	2005 0411

PRIORITY APPLN. INFO.: <-- AU 2000-21758 A3  
 1999  
 1213

AB A method of treating organic erectile dysfunction in a male comprises administering  
 apomorphine or its salt ester, or prodrug. Thus, sublingual tablets contained  
 apomorphine-HCl 2.00, mannitol 66.67, ascorbic acid 3.33, citric acid 2.00, Avicel PH  
 10215.00, Methocel E4 10.00, aspartame 0.67, and Mg stearate 0.33 weight%.

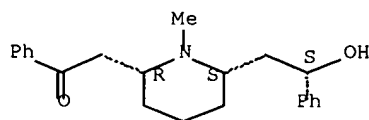
IT 134-64-5, Lobeline sulfate  
 RL: **THU (Therapeutic use)**; BIOL (Biological study); USES  
 (Uses)  
 (apomorphine for treatment of organic erectile dysfunction in  
 males)

RN 134-64-5 HCAPLUS  
 CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidiny]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 7664-93-9  
 CMF H2 O4 S



CM 2  
 CRN 90-69-7  
 CMF C22 H27 N O2

Absolute stereochemistry.



IC ICM A61K031-485  
 ICS A61P015-10  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1  
 IT 50-53-3, Chlorpromazine, biological studies 51-34-3, Scopolamine  
 54-11-5, Nicotine 58-38-8, Prochlorperazine 84-04-8,  
 Pipamazine 129-74-8, Buclizine hydrochloride 134-64-5,  
 Lobeline sulfate 138-56-7, Trimethobenzamide 303-25-3,  
 Cyclizine hydrochloride 364-62-5, Metoclopramide 523-87-5,  
 Dimenhydrinate 1420-55-9, Thiethylperazine 3254-89-5,  
 Diphenidol hydrochloride 14008-44-7, Metopimazine 17297-82-4,  
 Oxypendyl hydrochloride 57808-66-9, Domperidone 99614-02-5,  
 Ondansetron  
 RL: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (apomorphine for treatment of organic erectile dysfunction in  
 males)

L51 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:1311702 HCAPLUS Full-text  
 DOCUMENT NUMBER: 144:57525  
 TITLE: Coated vaginal devices for vaginal delivery of  
 therapeutically effective and/or  
 health-promoting agents  
 INVENTOR(S): Wilson, Michelle; Desai, Kishorkumar J.;  
 Pauletti, Giovanni M.; Antoon, Mitchell K.;  
 Clendenen, Chris E.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part  
 of U.S. Ser. No. 126,863  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent

10/813,647

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 11  
 PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
US 2005276836	A1	20051215	US 2005-180076	2005 0712
US 6197327	B1	20010306	<-- US 1998-79897	1998 0515
US 6086909	A	20000711	<-- US 1999-249963	1999 0212
US 6572874	B1	20030603	<-- US 2000-626025	2000 0727
NZ 508130	A	20020301	<-- NZ 2000-508130	2000 1113
AU 765269	B2	20030911	<-- AU 2001-54192	2001 0703
US 2003049302	A1	20030313	<-- US 2002-226667	2002 0821
US 6982091	B2	20060103		
US 2004005345	A1	20040108	US 2003-349029	2003 0122
US 6905701	B2	20050614	<--	
US 2004043071	A1	20040304	US 2003-600849	2003 0620
US 2005249774	A1	20051110	US 2005-126863	2005 0510
US 2006002966	A1	20060105	<-- US 2005-208209	2005 0818
PRIORITY APPLN. INFO.:			US 1997-49325P	P 1997 0611
			<-- US 1998-79897	A2 1998 0515
			<-- US 1999-249963	A2 1999 0212
			<-- US 2000-626025	A2 2000 0727
			US 2002-226667	A2

	2002 0821
US 2003-349029	A2 2003 0122
US 2003-600849	A2 2003 0620
US 2004-587454P	P 2004 0712
US 2005-126863	A2 2005 0510
AU 1998-76976	A3 1998 0610
<-- NZ 1998-502120	A1 1998 0610
<-- US 1999-146218P	P 1999 0728
<-- US 2001-315877P	P 2001 0829
US 2002-390748P	P 2002 0621

AB Disclosed is a vaginal device for delivering therapeutical and/or health-promoting agents. The vaginal device partly or completely coated by, covered by or combined with a coating or covering comprising a film, foam, strip, cap, cup or particles. The coating of the device comprises a mucoadhesive composition comprising a therapeutical and/or health-promoting agent. For example, sumatriptan vaginal suppository were prepared from Suppocire AS2X, hydroxypropyl Me cellulose as a mucoadhesive agent, and Transcutol as a permeation enhancer.

IT 90-69-7, Lobeline

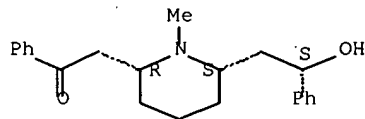
RL: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(coated vaginal devices for vaginal delivery of therapeutically effective and/or health-promoting agents)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidiny]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61F013-00

INCL 424422000

CC 63-6 (Pharmaceuticals)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies 50-21-5, Lactic acid, biological studies 50-23-7, Hydrocortisone 50-33-9, Phenylbutazone, biological studies 50-53-3, Chlorpromazine, biological studies 50-56-6, Oxytocin, biological studies 50-78-2, Acetylsalicylic acid 50-81-7, Ascorbic acid, biological studies 51-55-8, Atropine, biological studies 51-92-3, Tetramethylammonium 52-53-9, Verapamil 53-86-1, Indomethacin 55-63-0, Nitroglycerin 57-22-7, Vincristine 57-27-2, Morphine, biological studies 57-42-1, Meperidine 58-08-2, Caffeine, biological studies 58-33-3, Promethazine hydrochloride 58-38-8, Prochlorperazine 58-85-5, Biotin 59-02-9 59-05-2, Methotrexate 59-30-3, Folic acid, biological studies 59-43-8, Thiamine, biological studies 59-46-1, Procain 59-67-6, Niacin, biological studies 60-87-7, Promethazine 62-49-7, Choline 63-75-2, Arecoline 64-19-7, Acetic acid, biological studies 65-23-6, Pyridoxine 67-68-5, Dimethyl sulfoxide, biological studies 67-97-0, Cholecalciferol 68-04-2, Sodium citrate 68-19-9, Cyanocobalamin 76-99-3, Methadone 77-26-9, Butalbital 77-52-1, Ursolic acid 77-92-9, Citric acid, biological studies 79-83-4, D-Pantothenic acid 80-56-8,  $\alpha$ -Pinene 82-92-8, Cyclizine 83-88-5, Riboflavin, biological studies 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 89-78-1, Menthol 90-69-7, Lobeline 91-40-7, Fenamic acid 99-66-1, Valproic acid 103-90-2, Acetaminophen 111-90-0 113-15-5, Ergotamine 114-07-8, Erythromycin 127-09-3, Sodium acetate 127-91-3,  $\beta$ -Pinene 144-55-8, Sodium bicarbonate, biological studies 148-82-3, Mephalan 149-91-7, Gallic acid, biological studies 151-21-3, Sodium lauryl sulfate, biological studies 154-42-7, Thioguanine 302-79-4, Tretinoin 305-03-3, Chlorambucil 331-39-5, Caffeic acid 364-62-5, Metoclopramide 404-86-4, Capsaicin 439-14-5, Diazepam 443-48-1, Metronidazole 465-42-9, Capsanthin 469-21-6, Doxylamine 470-82-6, 1,8-Cineole 479-91-4, Casticin 479-98-1, Aucubin 497-19-8, Sodium carbonate, biological studies 499-04-7, Arecaine 503-01-5, Isometheptene 504-24-5, 4-Aminopyridine 506-26-3,  $\gamma$ -Linolenic acid 511-12-6, Dihydroergotamine 522-51-0, Dequalinium chloride 548-73-2, Droperidol 552-94-3, Salsalate 555-30-6, Methyldopa 564-25-0, Doxycycline 586-06-1, Metaproterenol 644-62-2 645-05-6, Altretamine 652-67-5, Isosorbide 671-16-9, Procarbazine 768-94-5, Amantadine 1156-19-0, Tolazamide 1330-80-9, Propylene glycol oleate 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1415-73-2, Aloin A 1951-25-3, Amiodarone 1972-08-3, Dronabinol 2022-85-7, Flucytosine 2751-09-9, Troleandomycin 2809-21-4 2854-38-8, Ergostine 2998-57-4, Estramustine 3056-17-5, Stavudine 3681-93-4, Vitexin 3930-20-9, Sotalol 4373-41-5, Maslinic acid 4547-24-4, Corosolic acid 4697-36-3, Carbenicillin 5051-62-7, Guanabenz 5104-49-4, Flurbiprofen 5300-03-8, Alitretinoin 5373-11-5, Luteolin 7-O-glucoside 6926-08-5, Harpagide 7232-21-5, Metoclopramide hydrochloride 7235-40-7,  $\beta$ -Carotene 7439-89-6, Iron, biological studies 7439-95-4, Magnesium, biological studies 7439-96-5, Manganese, biological studies 7440-09-7, Potassium, biological studies 7440-47-3, Chromium, biological studies 7440-66-6, Zinc, biological studies 7440-70-2, Calcium, biological studies 7481-89-2, Zalcitabine 7632-05-5, Sodium phosphate 7782-49-2, Selenium, biological studies 8025-81-8, Spiramycin 9000-69-5, Pectin 9002-64-6, Parathyroid hormone 9002-88-4, Polyethylene 9002-89-5, Polyvinyl alcohol 9002-92-0, Polyoxyethylene lauryl ether 9003-07-0, Polypropylene 9003-39-8, Polyvinylpyrrolidone 9003-97-8, Polycarbophil 9004-10-8, Insulin, biological studies 9005-37-2, Propylene glycol alginate 9005-38-3, Sodium alginate 9005-65-6, Tween 80 9007-12-9, Calcitonin 9010-79-1,

Ethylene-propylene copolymer 9012-76-4, Chitosan 10238-21-8,  
 Glyburide 10540-29-1, Tamoxifen 10596-23-3, Clodronate  
 11000-17-2, Vasopressin 11027-63-7, Agnoside 11076-50-9,  
 Tetramycin 12629-01-5, Human growth hormone 12650-69-0,  
 Mupirocin 13010-47-4, Lomustine 13392-28-4, Rimantadine  
 13710-19-5, Tolfenamic acid 15307-79-6, Diclofenac sodium  
 15307-86-5, Diclofenac 15663-27-1, Cisplatin 15686-71-2,  
 Cephalexin 15687-27-1, Ibuprofen 16051-77-7, Isosorbide  
 mononitrate 18323-44-9, Clindamycin 18559-94-9, Salbutamol  
 18642-44-9, Actein 19216-56-9, Prazosin 19236-22-7, Dinitrate  
 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22071-15-4,  
 Ketoprofen 22204-53-1, Naproxen 22494-42-4, Diflunisal  
 22916-47-8, Miconazole 23031-25-6, Terbutaline 23155-02-4,  
 Phosphomycin 23214-92-8, Doxorubicin 23593-75-1, Clotrimazole  
 24345-16-2, Apamin 25322-68-3, Polyethylene glycol 26171-23-3,  
 Tolmetin 26563-68-8, 3-epi-Maslinic acid 26652-09-5, Ritodrine  
 27220-47-9, Econazole 27523-40-6, Isoconazole 28371-16-6,  
 Aloin B 28608-75-5, Orientin 29110-47-2, Guanfacine  
 29342-05-0, Ciclopirox 29679-58-1, Fenoprofen 30516-87-1,  
 Zidovudine 30861-27-9, Aloeresin B 32619-42-4, Oleuropein  
 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34391-04-3,  
 Levalbuterol 35846-53-8, Maytansine 36322-90-4, Piroxicam  
 36791-04-5, Ribavirin 38194-50-2, Sulindac 38304-91-5,  
 Minoxidil 38677-81-5, Pirbuterol 38821-53-3, Cephadrine  
 38953-85-4, Isovitexin 39809-25-1, Penciclovir 40391-99-9  
 41340-25-4, Etodolac 42399-41-7, Diltiazem 42408-82-2,  
 Butorphanol 42924-53-8, Nabumetone 50370-12-2, Cefadroxil  
 50656-65-0, Rotundifuran 50972-17-3, Bacampicillin 51022-71-0,  
 Nabilone 51803-78-2, Nimesulide 53155-25-2, Euscaphic acid  
 54187-04-1, Rilmenidine 55268-75-2, Cefuroxime 55985-32-5,  
 Nicardipine 57186-25-1, Paxilline 57808-66-9, Domperidone  
 58799-57-8, Suppocire AS2X 59209-40-4, Afloxan 59277-89-3,  
 Acyclovir 59804-37-4, Tenoxicam 60142-96-3, Gabapentin  
 61263-49-8, Vitexilactone 61318-90-9, Sulconazole 62013-04-1,  
 Dirithromycin 63590-64-7, Terazosin 63612-50-0, Nilutamide  
 64104-39-8, Suppocire AM 64211-45-6, Oxiconazole 64706-54-3,  
 Bepridil 64872-76-0, Butoconazole 65277-42-1, Ketoconazole  
 65472-88-0, Naftifine 65899-73-2, Tioconazole 66085-59-4,  
 Nimodipine 66376-36-1, Alendronate 67915-31-5, Terconazole  
 68379-02-2, Clofilium

RL: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)

(coated vaginal devices for vaginal delivery of therapeutically  
 effective and/or health-promoting agents)

L51 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:2187 HCAPLUS Full-text

DOCUMENT NUMBER: 142:93692

TITLE: Preparation of 2,6-disubstituted piperidines  
 and piperazines for the treatment of  
 CNS diseases

INVENTOR(S): Crooks, Peter A.; Dwoskin, Linda; Jones,  
 Marlon D.; Miller, Dennis Keith; Norholm, Seth  
 Davin; Zheng, Guangrong; Krishnamurthy, Sairam

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part  
 of U.S. Ser. No. 231,156.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

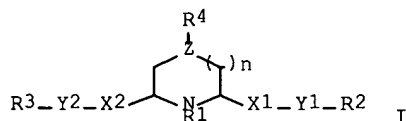
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004266824	A1	20041230	US 2004-813647	



				2004
				0331
			<--	
US 6455543	B1	20020924	US 2000-628557	
				2000
				0728
			<--	
US 2003100547	A1	20030529	US 2002-231156	
				2002
				0830
			<--	
US 6943177	B2	20050913		
PRIORITY APPLN. INFO.:			US 1999-146144P	P
				1999
				0730
			<--	
			US 2000-628557	A3
				2000
				0728
			US 2002-231156	A2
				2002
				0830

OTHER SOURCE(S): MARPAT 142:93692  
GI



AB Title compds. represented by the formula I [wherein X1 = CH2; Y1 = CHOH or C=O; X2-Y2 = cis/trans-carbon-carbon double bond; Z = CH; R1, R4 = independently H or alkyl; R2, R3 = independently (un)saturated hydrocarbon ring or (un)substituted benzene; n = 0-3; and pharmaceutically effective salts thereof, including resolved diastereomers, enantiomers thereof] were prepared. For example, lobelanidine was stirred overnight in 85% H3PO4 at 60° to give 78.6% cis-2,6-di-trans-styrylpiperidine. I showed activity in [3H]nicotine binding assay, [3H]MLA binding assay, inhibition of nicotine-evoked 86Rb+ efflux assay, and etc. Thus, I are useful to treat diseases of the **central nervous system, drug abuse**, and withdrawal therefrom as well as treating **eating disorders** (no data).

IT 324078-36-6P 324078-52-6P 752188-91-3P  
758717-83-8P 818377-08-1P

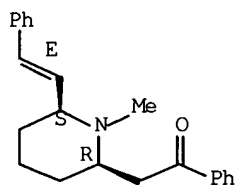
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2,6-disubstituted piperidines and piperazines for the **treatment of drug abuse** and withdrawal, **eating disorders**, and **CNS diseases**)

RN 324078-36-6 HCAPLUS

CN Ethanone, 2-[(2R,6S)-1-methyl-6-[(1E)-2-phenylethenyl]-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

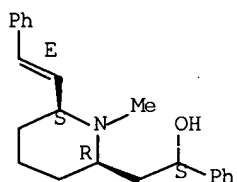
Absolute stereochemistry.  
Double bond geometry as shown.



RN 324078-52-6 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-[(1E)-2-phenylethenyl]-, ( $\alpha$ S,2R,6S)- (9CI) (CA INDEX NAME)

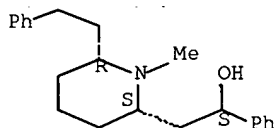
Absolute stereochemistry.  
Double bond geometry as shown.



RN 752188-91-3 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-, ( $\alpha$ S,2S,6R)- (9CI) (CA INDEX NAME)

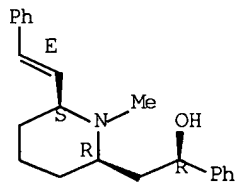
Absolute stereochemistry. Rotation (-).



RN 758717-83-8 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-[(1E)-2-phenylethenyl]-, ( $\alpha$ R,2R,6S)- (9CI) (CA INDEX NAME)

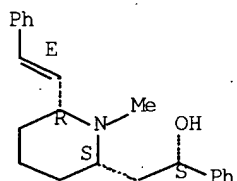
Absolute stereochemistry.  
Double bond geometry as shown.



RN 818377-08-1 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-[(1E)-2-phenylethenyl]-, ( $\alpha$ S,2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT 90-69-7P 552-72-7P 579-21-5P

324078-32-2P 324078-40-2P 324078-41-3P

748756-00-5P 818377-09-2P 818377-10-5P

818377-11-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

THU (Therapeutic use); BIOL (Biological study); PREP

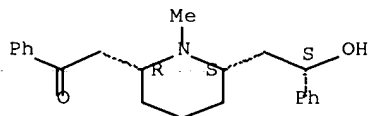
(Preparation); USES (Uses)

(preparation of 2,6-disubstituted piperidines and piperazines for the treatment of drug abuse and withdrawal, eating disorders, and CNS diseases)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

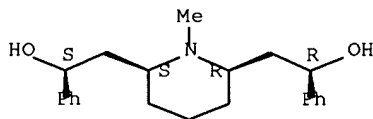
Absolute stereochemistry.



RN 552-72-7 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-, ( $\alpha$ R, $\alpha'$ S,2R,6S)-rel- (9CI) (CA INDEX NAME)

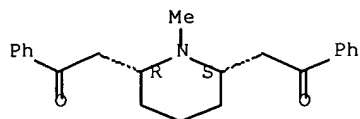
Relative stereochemistry.



RN 579-21-5 HCAPLUS

CN Ethanone, 2,2'-(1-methyl-2,6-piperidinediyl)bis[1-phenyl-, (2R,6S)-rel- (9CI) (CA INDEX NAME)

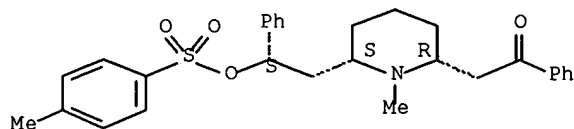
Relative stereochemistry.



RN 324078-32-2 HCAPLUS

CN Ethanone, 2-[(2R,6S)-1-methyl-6-[(2S)-2-[[4-methylphenyl)sulfonyl]oxy]-2-phenylethyl]-2-piperidiny]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

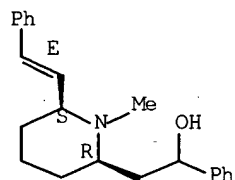


RN 324078-40-2 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-[(1E)-2-phenylethenyl]-, (2R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

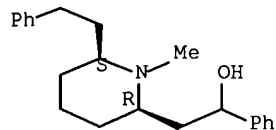
Double bond geometry as shown.



RN 324078-41-3 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-, (2R,6S)- (9CI) (CA INDEX NAME)

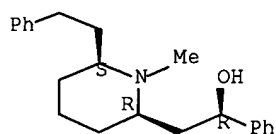
Absolute stereochemistry.



RN 748756-00-5 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-, ( $\alpha$ R,2R,6S)- (9CI) (CA INDEX NAME)

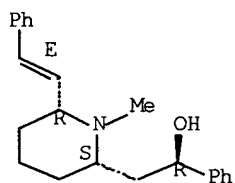
Absolute stereochemistry. Rotation (+).



RN 818377-09-2 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-[(1E)-2-phenylethenyl]-, ( $\alpha$ R,2S,6R)- (9CI) (CA INDEX NAME)

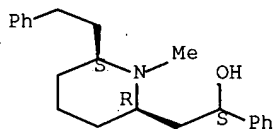
Absolute stereochemistry.  
Double bond geometry as shown.



RN 818377-10-5 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-, ( $\alpha$ S,2R,6S)- (9CI) (CA INDEX NAME)

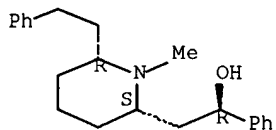
Absolute stereochemistry. Rotation (-).



RN 818377-11-6 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-, ( $\alpha$ R,2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-445

ICS C07D211-20

INCL 514317000; 546236000; 546237000

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

ST piperidine piperazine prepn CNS drug

- abuse eating disorder treatment**
- IT **Drugs of abuse**  
(**abuse** of; preparation of 2,6-disubstituted piperidines and piperazines for the **treatment** of **drug abuse** and withdrawal, **eating disorders**, and **CNS** diseases)
- IT **Central nervous system, disease**  
Drug withdrawal  
**Eating disorders**  
(preparation of 2,6-disubstituted piperidines and piperazines for the **treatment** of **drug abuse** and withdrawal, **eating disorders**, and **CNS** diseases)
- IT **324078-36-6P 324078-52-6P 752188-91-3P**  
**758717-83-8P 758717-85-0P 758717-86-1P**  
**818377-08-1P 818377-12-7P**  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of 2,6-disubstituted piperidines and piperazines for the **treatment** of **drug abuse** and withdrawal, **eating disorders**, and **CNS** diseases)
- IT **90-69-7P 530-51-8P 552-72-7P 579-21-5P**  
**324078-19-5P 324078-32-2P 324078-40-2P**  
**324078-41-3P 650636-96-7P 748756-00-5P**  
**818377-09-2P 818377-10-5P 818377-11-6P**  
818377-13-8P 818377-14-9P 818377-15-0P 818377-16-1P  
818377-17-2P 818377-18-3P 818377-19-4P 818377-20-7P  
818377-21-8P 818377-22-9P 818377-23-0P 818377-24-1P  
818377-25-2P 818377-26-3P 818377-27-4P 818377-28-5P  
818377-29-6P 818377-30-9P 818377-31-0P 818377-32-1P  
818377-33-2P 818377-34-3P 818377-35-4P 818377-36-5P  
818377-37-6P 818377-38-7P 818377-39-8P 818377-40-1P  
818377-41-2P 818377-42-3P 818377-43-4P 818377-44-5P  
818377-45-6P 818377-46-7P 818377-47-8P 818377-48-9P  
818377-49-0P 818377-50-3P 818377-51-4P 818377-52-5P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of 2,6-disubstituted piperidines and piperazines for the **treatment** of **drug abuse** and withdrawal, **eating disorders**, and **CNS** diseases)
- IT 108-48-5, 2,6-Lutidine 134-64-5 620-08-6, 4-Methoxypyridine  
3277-89-2, 2-Phenylethylmagnesium bromide 6738-06-3,  
Phenylethynylmagnesium bromide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of 2,6-disubstituted piperidines and piperazines for the **treatment** of **drug abuse** and withdrawal, **eating disorders**, and **CNS** diseases)
- IT 818377-53-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 2,6-disubstituted piperidines and piperazines for the **treatment** of **drug abuse** and withdrawal, **eating disorders**, and **CNS** diseases)

L51 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2002:482981 HCAPLUS Full-text  
DOCUMENT NUMBER: 137:52376  
TITLE: Treatment and system for nicotine withdrawal  
INVENTOR(S): Reynolds, Mark  
PATENT ASSIGNEE(S): USA

10/813,647

SOURCE: U.S., 10 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6409991	B1	20020625	US 1999-464549	1999 1215
US 6645470	B1	20031111	US 2002-72822	2002 0208

PRIORITY APPLN. INFO.: <--  
 US 1999-464549 A1  
 1999  
 1215

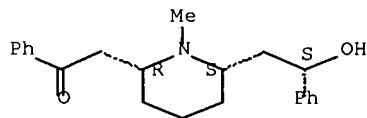
AB A kit and associated method in which symptoms of nicotine withdrawal syndrome are relieved as well as addressing the associated weight gain issues and craving for sweets by combining nicotine replacement therapy with complementary dosages of xylitol. A kit comprises multiple pieces of a nicotine gum containing 2-4 mg of nicotine or its metabolite and a nicotine-free xylitol gum containing at least 670 mg xylitol.

IT 90-69-7, Lobeline  
 RL: PAC (Pharmacological activity); THU (Therapeutic use)  
 ; BIOL (Biological study); USES (Uses)  
 (kits containing nicotine gum and xylitol gum for treatment of nicotine withdrawal and associated symptoms)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K009-68  
 ICS A61K031-465  
 INCL 424048000  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1

IT 54-11-5, Nicotine 54-11-5D, Nicotine, metabolites, salts  
 90-69-7, Lobeline  
 RL: PAC (Pharmacological activity); THU (Therapeutic use)  
 ; BIOL (Biological study); USES (Uses)  
 (kits containing nicotine gum and xylitol gum for treatment of nicotine withdrawal and associated symptoms)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L51 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2001:312496 HCAPLUS Full-text  
 DOCUMENT NUMBER: 134:316097  
 TITLE: Antinicotinic preparation  
 INVENTOR(S): Gonzalez Manzanares, Jesus Maria  
 PATENT ASSIGNEE(S): Spain

SOURCE: Span., 5 pp.  
 CODEN: SPXXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Spanish  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2141024	A1	20000301	ES 1997-2063	1997 1003
ES 2141024	B1	20001016	ES 1997-2063	1997 1003

PRIORITY APPLN. INFO.: <--

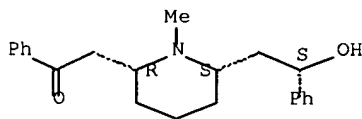
AB An antinicotinic preparation is disclosed which contains a carrier polymer which biol. is resorbed and which contains groups of metabolic cations modified by alkaloids such as anabasine, cytisine, lobeline, or other antinicotinic agent. The carrier polymer may be monocarboxymethyl cellulose, CM-cellulose, cellulose phosphate, polymethacrylic acid, polyvinyl sulfate, albumin oxide, or dicarboxyldextran. The preparation may be used to help stop smoking.

IT 90-69-7, Lobeline  
 RL: PEP (Physical, engineering or chemical process); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process);  
 USES (Uses)  
 (antinicotinic preparation for cessation of smoking)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-445

ICS A61K009-68

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 4

IT 57-50-1, Sucrose, biological studies 90-69-7, Lobeline  
 485-35-8, Cytisine 9004-32-4, Carboxymethyl cellulose  
 9004-54-0D, Dextran, carboxy derivs., biological studies  
 9015-14-9, Cellulose phosphate 15251-47-5, Anabasine  
 hydrochloride 25087-26-7, Polymethacrylic acid 25191-25-7,  
 Polyvinyl sulfate

RL: PEP (Physical, engineering or chemical process); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process);  
 USES (Uses)

(antinicotinic preparation for cessation of smoking)

L51 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:224392 HCAPLUS Full-text

DOCUMENT NUMBER: 134:247256

TITLE: Dextromethorphan and oxidase inhibitor for  
 weaning patients from narcotics and  
 antidepressants

INVENTOR(S): Smith, Richard A.



10/813,647

PATENT ASSIGNEE(S): USA  
 SOURCE: U.S., 9 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6207674	B1	20010327	US 1999-471060	1999 1222
CA 2395411	AA	20010628	CA 2000-2395411	2000 1222
WO 2001045708	A1	20010628	WO 2000-US34967	2000 1222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1239860	A1	20020918	EP 2000-990294	2000 1222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518063	T2	20030603	JP 2001-546647	2000 1222
AU 774847	B2	20040708	AU 2001-27338	2000 1222
RU 2281771	C2	20060820	RU 2002-115659	2000 1222
EP 1700601	A2	20060913	EP 2006-111654	2000 1222
EP 1700601	A3	20060927		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
AU 2004200969	A1	20040401	AU 2004-200969	2004 0305
AU 2005225081	A1	20051110	AU 2005-225081	2005 1020
PRIORITY APPLN. INFO.: US 1999-471060 A				

<--

AU 2001-27338	A3	2000
		1222
EP 2000-990294	A3	2000
		1222
WO 2000-US34967	W	2000
		1222

AB Patients can be helped to break free of addictive or habit-forming narcotics and antidepressants, by **treatment** using two **drugs**. One drug is dextromethorphan (DM), which has been used for decades as an antitussive (cough-suppressing) drug in cough syrups. The other drug is an oxidase inhibitor which suppresses activity of a liver enzyme called cytochrome P 450-2D6 (also called debrisoquin hydroxylase, sparteine monooxygenase, cytochrome P 450-DB, and CYP2D6). In most patients, this oxidase rapidly degrades DM and converts it into a metabolite called dextrorphan. An oxidase inhibitor (such as quinidine) which suppresses cytochrome P 450-2D6 activity increases the half-life and concentration of DM in the circulating blood. When this combined treatment was administered orally to patients who had become dependent on morphine and anti-depressant drugs because of chronic intractable pain, it initially helped the patients reduce their dosages of morphine and other drugs, including antidepressants. When addnl. testing was done, the combined treatment allowed patients to entirely terminate all use of morphine and antidepressants, with minimal withdrawal or other adverse effects. Importantly, these same patients received no substantial benefit from taking DM by itself, without an oxidase inhibitor. Accordingly, the combination of dextromethorphan plus an anti-oxidase drug can allow at least some patients to break entirely free of narcotics and/or antidepressants, even after years of use for chronic pain and other medical problems, even when they are not substantially helped by dextromethorphan alone.

IT 90-69-7, Lobeline 90-69-7D, Lobeline, isomers

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use);

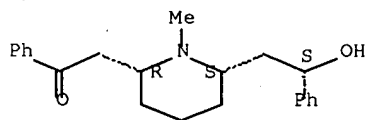
BIOL (Biological study); USES (Uses)

(dextromethorphan and oxidase inhibitor for weaning patients from narcotics and antidepressants)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

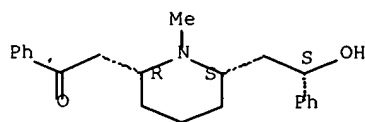
Absolute stereochemistry.



RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-44  
ICS A61K031-27; A61K031-135  
INCL 514289000  
CC 1-11 (Pharmacology)  
ST **narcotic analgesic addiction treatment**  
dextromethorphan oxidase inhibitor; CYP2D6 inhibitor  
dextromethorphan **narcotic analgesic addiction**  
**treatment**  
IT 50-53-3, Chlorpromazine, biological studies 50-53-3D,  
Chlorpromazine, isomers 52-86-8, Haloperidol 52-86-8D,  
Haloperidol, isomers 56-54-2, Quinidine 58-73-1,  
Diphenhydramine 58-73-1D, Diphenhydramine, isomers 58-74-2,  
Papaverine 58-74-2D, Papaverine, isomers 72-69-5,  
Nortriptyline 72-69-5D, Nortriptyline, isomers **90-69-7**  
, Lobeline **90-69-7D**, Lobeline, isomers 125-71-3,  
Dextromethorphan 130-95-0, Quinine 130-95-0D, Quinine, isomers  
146-48-5, Yohimbine 146-48-5D, Yohimbine, isomers 525-66-6,  
Propranolol 525-66-6D, Propranolol, isomers 1893-33-0,  
Pipamperone 1893-33-0D, Pipamperone, isomers 4360-12-7,  
Ajmaline 4360-12-7D, Ajmaline, isomers 6452-71-7, Oxprenolol  
6452-71-7D, Oxprenolol, isomers 26839-75-8, Timolol  
26839-75-8D, Timolol, isomers 27203-92-5, Tramadol 31828-71-4,  
Mexiletine 31828-71-4D, Mexiletine, isomers 36894-69-6,  
Labetalol 36894-69-6D, Labetalol, isomers 51384-51-1  
51384-51-1D, isomers 54910-89-3, Fluoxetine 54910-89-3D,  
Fluoxetine, isomers 57808-66-9, Domperidone 57808-66-9D,  
Domperidone, isomers 60142-96-3, Neurontin  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); **THU (Therapeutic use)**;  
BIOL (Biological study); USES (Uses)  
(dextromethorphan and oxidase inhibitor for weaning patients  
from narcotics and antidepressants)  
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2001:100973 HCAPLUS Full-text  
DOCUMENT NUMBER: 134:147501  
TITLE: Preparation of cis-2,6-disubstituted  
piperidines for the treatment of  
psychostimulant abuse and withdrawal,  
**eating disorders, and**  
**central nervous**  
**system** diseases and pathologies.  
INVENTOR(S): Dwoskin, Linda P.; Crooks, Peter A.; Jones,  
Marlon D.  
PATENT ASSIGNEE(S): University of Kentucky Research Foundation,  
USA  
SOURCE: PCT Int. Appl., 28 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2001008678	A1	20010208	WO 2000-US20553	2000 0728

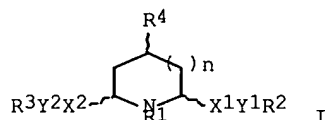
&lt;--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,  
CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE,  
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC,

10/813,647

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
 TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,  
 CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,  
 SN, TD, TG  
 AU 2000063867 A5 20010219 AU 2000-63867 2000  
 0728  
 <--  
 EP 1513513 A1 20050316 EP 2000-950822 2000  
 0728  
 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
 MC, PT, IE, FI, CY  
 PRIORITY APPLN. INFO.: US 1999-146144P P 1999  
 0730  
 <--  
 WO 2000-US20553 W 2000  
 0728

OTHER SOURCE(S): MARPAT 134:147501  
 GI



AB A method for **treatment** of **drug** dependence, drug withdrawal, an **eating disorder**, or a **CNS** disease or pathol. comprises administration of title compds. [I; n = 0-3; X1Y1, X2Y2 = C-C single, double, or triple bond, C-S bond, C-Se bond, C-O bond, (N-alkyl) C-N single or double bond, N-N double bond; R1, R4 = H, alkyl; R1R4 = atoms to form a ring including CH2, CH2CH2, (CH2)3, cis-CH:CH, cis-CH2CH:CH; R2, R3 = (unsatd.) hydrocarbon ring, N-, O-, S-, and/or Se-containing heterocyclyl, o-, m-, or p-substituted benzene; with provisos]. Thus, lobelanidine was stirred overnight in 85% H3PO4 at 60° to give 78.6% cis-2,6-di-trans- styrylpiperidine. Tested I showed Ki = 0.0043 μM to ≥100 μM in the high affinity [3H] nicotine binding assay.

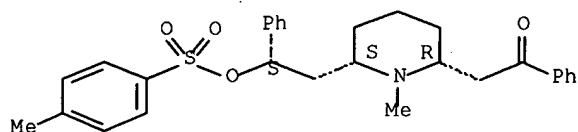
IT 324078-32-2P 324078-36-6P 324078-40-2P  
 324078-41-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)

RN 324078-32-2 HCAPLUS

CN. Ethanone, 2-[(2R,6S)-1-methyl-6-[(2S)-2-[(4-methylphenyl)sulfonyl]oxy]-2-phenylethyl]-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

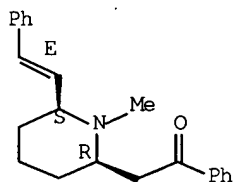
Absolute stereochemistry.



RN 324078-36-6 HCAPLUS

CN Ethanone, 2-[(2R,6S)-1-methyl-6-[(1E)-2-phenylethenyl]-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

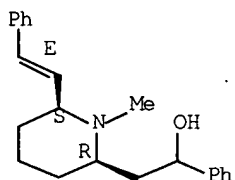
Absolute stereochemistry.  
Double bond geometry as shown.



RN 324078-40-2 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-[(1E)-2-phenylethenyl]-, (2R,6S)- (9CI) (CA INDEX NAME)

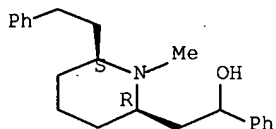
Absolute stereochemistry.  
Double bond geometry as shown.



RN 324078-41-3 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-, (2R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-33

ICS A61K031-40; A61K031-445; A61K031-55; C07D207-08; C07D207-10;  
C07D207-12; C07D207-14; C07D207-16; C07D211-18; C07D211-20;

C07D211-22; C07D211-24; C07D211-26; C07D211-30; C07D211-32;  
C07D225-00

- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
- ST piperidine **drug abuse eating disorder** nervous system disease treatment; lobeline analog **drug abuse eating disorder** nervous system disease; dopamine reuptake inhibitor piperidine lobeline analog prepn; nicotinic receptor antagonist piperidine lobeline analog; transporter protein dopamine inhibitor piperidine lobeline analog prepn
- IT Brain, disease  
(Gilles de la Tourette syndrome, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Nervous system  
(Huntington's chorea, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT **Drugs of abuse**  
(**abuse** of, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Mental disorder  
(attention deficit disorder, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Mental disorder  
(attention deficit hyperactivity disorder, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT **Nervous system**  
(**central**, disease, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Memory, biological  
(disorder, treatment of memory loss; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Appetite  
Sleep  
(disorder, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Transport proteins  
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
(dopamine-transporting, inhibitors; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous**

- system** diseases and pathologies)
- IT Sleep  
(narcolepsy, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Mental disorder  
(obsession-compulsion, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Anxiety  
(panic disorder, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Anti-Alzheimer's agents  
Antidepressants  
Antiparkinsonian agents  
Antipsychotics  
Cognition enhancers  
Nicotinic antagonists  
(preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Brain, disease  
(trauma, treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Fatigue, biological  
(treatment of chronic nervous exhaustion; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT Motion sickness  
Myasthenia gravis  
(treatment; preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT 90-69-7, Lobeline 324078-50-4 324078-52-6  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT 324078-19-5P 324078-32-2P 324078-36-6P 324078-40-2P 324078-41-3P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating disorders**, and **central nervous system** diseases and pathologies)
- IT 552-72-7, Lobelanidine 6266-38-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, **eating**

**disorders, and central nervous  
system diseases and pathologies)**

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2000:790171 HCAPLUS Full-text  
DOCUMENT NUMBER: 133:350144  
TITLE: Pyridine and piperidine derivatives for  
treating neurodegenerative diseases  
INVENTOR(S): Meth-Cohn, Otto; Yu, Chu-Yi; Lestage, Pierre;  
Lebrun, Marie-Cecile; Caignard, Daniel-Henri;  
Renard, Pierre  
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.; Les Laboratoires  
Servier  
SOURCE: Eur. Pat. Appl., 36 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1050531	A1	20001108	EP 2000-401198	2000 0502
<--				
EP 1050531	B1	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
FR 2793245	A1	20001110	FR 1999-5690	1999 0505
FR 2793245	B1	20021011		
CN 1277192	A	20001220	CN 2000-118157	2000 0430
<--				
JP 2000355579	A2	20001226	JP 2000-133762	2000 0502
<--				
JP 3533361	B2	20040531		
JP 2002179652	A2	20020626	JP 2001-319183	2000 0502
<--				
AT 282595	E	20041215	AT 2000-401198	2000 0502
<--				
PT 1050531	T	20050331	PT 2000-401198	2000 0502
<--				
ES 2233302	T3	20050616	ES 2000-401198	2000 0502
<--				
NO 2000002351	A	20001106	NO 2000-2351	2000 0504
<--				
NO 317095	B1	20040809		



10/813,647

NZ 504338	A	20010629	NZ 2000-504338	2000 0504
			<--	
US 6323220	B1	20011127	US 2000-564527	2000 0504
			<--	
CA 2308867	AA	20001105	CA 2000-2308867	2000 0505
			<--	
CA 2308867	C	20060314		
ZA 2000002207	A	20001114	ZA 2000-2207	2000 0505
			<--	
BR 2000002287	A	20010102	BR 2000-2287	2000 0505
			<--	
AU 764388	B2	20030814	AU 2000-32552	2000 0505
			<--	
US 2002035123	A1	20020321	US 2001-963018	2001 0925
			<--	
US 6511992	B2	20030128		
US 2002040036	A1	20020404	US 2001-962376	2001 0925
			<--	
US 6638946	B2	20031028		
US 2003139408	A1	20030724	US 2002-306024	2002 1127
			<--	
US 6734196	B2	20040511		
US 2003181484	A1	20030925	US 2003-377843	2003 0303
			<--	
US 2005004168	A1	20050106	US 2004-844856	2004 0513
			<--	
US 2006211731	A1	20060921	US 2006-438169	2006 0522
			<--	
PRIORITY APPLN. INFO.:			FR 1999-5690	A 1999 0505
			<--	
			JP 2000-133762	A3 2000 0502
			US 2000-564527	A3 2000 0504
			US 2001-963018	A1 2001 0925

US 2003-377843

B1

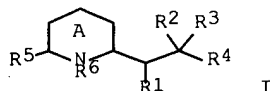
2003  
0303

US 2004-844956

A1

2004  
0512

OTHER SOURCE(S): MARPAT 133:350144  
GI



AB Title compds. I [R1 = H; R1R4 = atoms required to complete a 6-membered ring; R1R2 = bond; R2 = H, R3 = OH; R2R3 = O; R3 = 5- or 6-membered N heterocycle; R4 = (un)substituted Ph, naphthyl, heteroaryl; R5 = 5- or 6-membered N heterocycle which may contain other heteroatoms, CHR1', CR2'R3'R4' where R1'-R4' have the same definitions as R1-R4; R6 = H, alkyl; ring = pyridine, pyridinium, piperidine] were prepared for use in treating neurodegenerative diseases and pain (no data). Thus, 2-fluoropyridine is quaternized with 4-MeC6H4SO3Me, treated with 4-bromoacetophenone pyrrolidine enamine, and reduced to 2-(1-methyl-2-piperidinyl)-1- (4-bromophenyl)-1-ethanone HI.

IT 304680-14-6P 304680-15-7P 304680-16-8P

304680-17-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use);

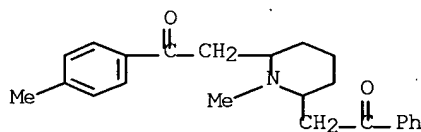
BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridine and piperidine derivs. for treating

neurodegenerative diseases)

RN 304680-14-6 HCAPLUS

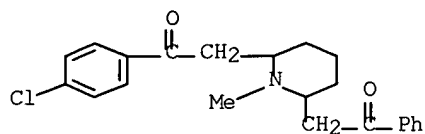
CN Ethanone, 2-[1-methyl-6-[2-(4-methylphenyl)-2-oxoethyl]-2-piperidinyl]-1-phenyl-, hydriodide (9CI) (CA INDEX NAME)



● HI

RN 304680-15-7 HCAPLUS

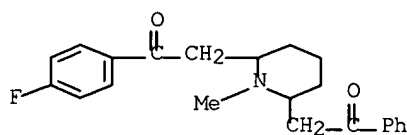
CN Ethanone, 1-(4-chlorophenyl)-2-[1-methyl-6-(2-oxo-2-phenylethyl)-2-piperidinyl]-, hydriodide (9CI) (CA INDEX NAME)



● HI

RN 304680-16-8 HCAPLUS

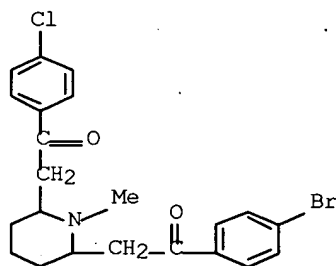
CN Ethanone, 1-(4-fluorophenyl)-2-[1-methyl-6-(2-oxo-2-phenylethyl)-2-piperidinyl]-, hydriodide (9CI) (CA INDEX NAME)



● HI

RN 304680-17-9 HCAPLUS

CN Ethanone, 1-(4-bromophenyl)-2-[6-[2-(4-chlorophenyl)-2-oxoethyl]-1-methyl-2-piperidinyl]-, hydriodide (9CI) (CA INDEX NAME)



● HI

IC ICM C07D213-50

ICS C07D213-30; C07D211-22; C07D211-32; C07D213-36; C07D401-06;  
A61K031-435; A61P025-28

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT	263017-15-8P	304679-66-1P	304679-82-1P	304679-83-2P
	304679-85-4P	304679-86-5P	304679-87-6P	304679-88-7P
	304679-89-8P	304679-90-1P	304679-92-3P	304679-93-4P
	304679-95-6P	304679-96-7P	304679-98-9P	304680-10-2P
	304680-13-5P	<b>304680-14-6P</b>	<b>304680-15-7P</b>	
	<b>304680-16-8P</b>	<b>304680-17-9P</b>	304680-18-0P	
	304680-19-1P	304680-22-6P	304680-23-7P	304680-24-8P
	304680-26-0P	304680-27-1P	304680-28-2P	304680-29-3P
	304680-30-6P	304680-31-7P	304680-32-8P	304680-33-9P
	304680-34-0P	304874-24-6P	304874-25-7P	

RL: SPN (Synthetic preparation); THU (Therapeutic use);

10/813,647

BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of pyridine and piperidine derivs. for treating  
neurodegenerative diseases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2000:756906 HCAPLUS Full-text  
DOCUMENT NUMBER: 133:317529  
TITLE: Method for screening compounds using nematode  
worms  
INVENTOR(S): Feichtinger, Richard; Rottiers, Veerle;  
Bogaert, Thierry; Maillet, Isabelle  
PATENT ASSIGNEE(S): Devgen N.V., Belg.  
SOURCE: PCT Int. Appl., 26 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000063424	A2	20001026	WO 2000-IB554	2000 0414

<--

WO 2000063424 A3 20010208  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,  
CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE,  
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN,  
TD, TG

CA 2369734	AA	20001026	CA 2000-2369734	2000 0414
------------	----	----------	-----------------	--------------

<--

GB 2350896	A1	20001213	GB 2000-9364	2000 0414
------------	----	----------	--------------	--------------

<--

GB 2350896	B2	20010425		
EP 1169471	A2	20020109	EP 2000-919099	2000 0414

<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT, IE, SI, LT, LV, FI, RO  
JP 2002542464 T2 20021210 JP 2000-612501  
2000  
0414

<--

HK 1030450	A1	20010817	HK 2001-100798	2001 0205
------------	----	----------	----------------	--------------

<--

PRIORITY APPLN. INFO.: GB 1999-8676 A  
1999  
0415

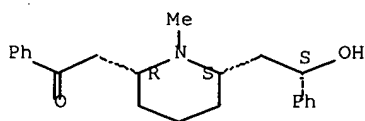
AB The invention provides improved methods of screening compds. for potential pharmacol. activity using nematode worms, principally but not exclusively, *Caenorhabditis elegans*. Specifically, the invention relates to methods in which the test compound is added directly to a nematode food source organism (e.g. a microorganism) and therefore taken up by the nematodes during feeding.

IT **90-69-7, Lobeline**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**;  
 BIOL (Biological study); USES (Uses)  
 (compound screening method using nematode worm)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C12Q001-02  
 ICS C12Q001-18; C12N001-20; C12N001-20; C12R001-19

CC 1-1 (**Pharmacology**)

IT 54-11-5, Nicotine 57-47-6, Physostigmine **90-69-7**,  
 Lobeline 465-65-6, Naloxone 1744-22-5, Riluzole 10540-29-1,  
 Tamoxifen 14769-73-4, Levamisole 15500-66-0, Pancuronium  
 54910-89-3, Fluoxetine 65595-90-6, W7 67526-95-8, Thapsigargin  
 74050-98-9, Ketanserin  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**;  
 BIOL (Biological study); USES (Uses)  
 (compound screening method using nematode worm)

L51 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:560344 HCAPLUS Full-text

DOCUMENT NUMBER: 133:329442

TITLE: Lobeline: Implications for nicotinic pharmacophore models

AUTHOR(S): Flammia, Dwight David, II

CORPORATE SOURCE: Virginia Commonwealth University, USA

SOURCE: (1999) 159 pp. Avail.: UMI, Order No. DA9950371  
 From: Diss. Abstr. Int., B 2000, 60(11), 5533

DOCUMENT TYPE: Dissertation

LANGUAGE: English

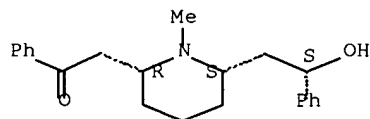
AB Unavailable

IT **90-69-7, Lobeline**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**;  
 BIOL (Biological study); USES (Uses)  
 (lobeline in implications for nicotinic pharmacophore models)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 1-12 (**Pharmacology**)IT **90-69-7**, LobelineRL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); **THU (Therapeutic use)**;

BIOL (Biological study); USES (Uses)

(lobeline in implications for nicotinic pharmacophore models)

L51 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:553442 HCAPLUS Full-text

DOCUMENT NUMBER: 133:168383

TITLE: Pharmaceutical compositions containing  
nicotine or a ligand of nicotine receptors and  
a monamine oxidase inhibitor and their use for  
treating tobacco withdrawal symptomsINVENTOR(S): Caille, Dominique; George, Pascal; Jegham,  
Samir; Robineau, Pascale; Scatton, Bernard;  
Zivkovic, Branimir

PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045846	A1	20000810	WO 2000-FR193	2000 0128

&lt;--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,  
CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM,  
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,  
MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN,  
TD, TG

FR 2788982	A1	20000804	FR 1999-1144	1999 0202
------------	----	----------	--------------	--------------

FR 2788982	B1	20020802		
CA 2361437	AA	20000810	CA 2000-2361437	2000 0128

&lt;--

EP 1150715	A1	20011107	EP 2000-901660	2000 0128
------------	----	----------	----------------	--------------

&lt;--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT, IE, SI, LT, LV, FI, RO  
JP 2002536342 T2 20021029 JP 2000-596965

2000

0128

PRIORITY APPLN. INFO.:

<--  
FR 1999-1144

A

1999

0202

<--  
WO 2000-FR193

W

2000

0128

OTHER SOURCE(S): MARPAT 133:168383

AB The invention concerns novel pharmaceutical compns. containing nicotine or a ligand of nicotine receptors and a monamine oxidase inhibitor designed for treating tobacco withdrawal symptoms. A bilayer tablet contained befloxadone 5, lactose 66, microcryst. cellulose 20, povidone 4, crospovidone 4, and magnesium stearate 1% in the first layer, and nicotine polarcirlex 5, microcryst. cellulose 20 povidone 4, hydroxypropyl Me cellulose 25, magnesium stearate 1, and lactose q.s. 100% in the second layer.

IT 90-69-7, Lobelin

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use);

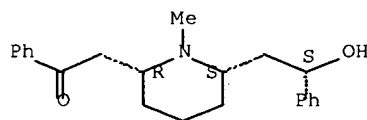
BIOL (Biological study); USES (Uses)

(pharmaceutical compns. containing nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K045-06

ICS A61K031-535; A61K031-465; A61K031-42

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT 54-11-5, Nicotine 90-69-7, Lobelin 262-20-4,  
Phenoxathiin 357-70-0, Galantamine 485-35-8, Cytisine  
538-79-4, Metanicotine 555-57-7, Pargyline 14611-51-9,  
L-Deprenyl 15585-43-0, RJR 2403 18464-39-6, Caroxazone  
29218-27-7, Toloxatone 60762-57-4, Pirlindole 63638-91-5,  
Brofaromine 64840-90-0, Eperisone 71320-77-9, Moclobemide  
75603-31-5, An 072 76990-56-2, Milacemide 77518-07-1,  
Amiflamine 91406-11-0, Esuprone 93438-65-4, Conantokin g  
94011-82-2, Bazinaprime 103878-84-8, Lazabemide 105365-76-2,  
Rs8359 117854-28-1, Befol 119386-96-8, Mofegiline  
134564-82-2, Befloxadone 135204-83-0, t794 136236-51-6,  
Rasagiline 140111-52-0, Epibatidine 147402-53-7, Abt-418  
150366-18-0, e 2011 156137-99-4, Rapacuronium bromide  
156223-05-1, Gts-21 161416-98-4, a 85380 161417-03-4, Abt 089  
164523-00-6 176773-68-5 176773-86-7 178419-47-1, AR-R 17779  
179120-92-4, Altinicline 189439-39-2 189439-83-6 189439-84-7  
190733-42-7 190733-47-2 190733-50-7 190789-14-1  
190789-52-7 191611-76-4, Sib 1553a 195211-53-1, Dbo 83  
198283-73-7, Abt 594 205187-44-6, KP 9 207391-08-0  
207391-13-7 207391-21-7 207391-34-2 207391-48-8  
207391-53-5 213998-46-0, GW 280430 214189-84-1 214189-85-2  
214901-35-6 215367-30-9 215367-49-0 215367-62-7  
215367-72-9 216579-65-6 216579-73-6 216580-87-9

10/813,647

216581-23-6	216581-38-3	216853-05-3	216853-29-1
216853-36-0	216970-31-9	216970-32-0	216970-33-1
220100-50-5	223795-00-4	223796-26-7	223796-36-9
223796-52-9	223797-21-5	223797-32-8	224818-46-6
287973-22-2	287973-23-3	287973-24-4	287973-25-5
287973-26-6	287973-27-7	287973-28-8	287973-29-9
287973-30-2	287973-31-3	287973-32-4	287973-33-5
287980-52-3, RJR 2531	287980-53-4, RJR 2557		

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); **THU (Therapeutic use)**;

BIOL (Biological study); USES (Uses)

(pharmaceutical compns. containing nicotine or ligand of nicotine  
receptors and monamine oxidase inhibitor and their use for  
treating tobacco withdrawal symptoms)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:467867 HCAPLUS Full-text

DOCUMENT NUMBER: 133:84292

TITLE: Use of lobeline compounds in the treatment of  
**central nervous**

**system** diseases and pathologies

INVENTOR(S): Crooks, Peter A.; Dwoskin, Linda P.

PATENT ASSIGNEE(S): University of Kentucky Research Foundation,  
USA

SOURCE: U.S., 31 pp., Cont.-in-part of U.S. 5,830904.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	
US 6087376	A	20000711	US 1998-89420	1998 0603
			<--	
US 5830904	A	19981103	US 1997-795852	1997 0205
			<--	
PRIORITY APPLN. INFO.:			US 1997-795852	A2 1997 0205
			<--	

OTHER SOURCE(S): MARPAT 133:84292

AB Lobeline and nicotine evoke [3H]overflow from rat striatal slices preloaded with [3H]dopamine ([3H]DA). The lobeline-evoked overflow is calcium-independent and not antagonized by mecamylamine, suggesting a mechanism of action other than the stimulation of nicotinic receptors. Whereas nicotine stimulates nicotinic receptors, lobeline inhibits [3H]DA uptake into synaptic vesicles and striatal synaptosomes. The results suggest that different mechanisms are responsible for the increase in striatal DA release evoked by lobeline and nicotine. [3H]- Dihydrotetrabenazine ([3H]DTBZ), used routinely to probe a high-affinity binding site-on the vesicular monoamine transporter (VMAT2) binds to vesicle membranes from rat striatum. Lobeline inhibits [3H]DTBZ binding with an IC50 of 0.90  $\mu$ M, consistent with its IC50 of 0.88  $\mu$ M for inhibition of [3H]DA uptake into vesicles. These results suggest that the action of lobeline is similar to that of amphetamine and that it specifically interacts with DTBZ sites on VMAT2 to inhibit DA uptake into synaptic vesicles. d-amphetamine inhibits [3H]DTBZ binding to vesicle membranes with an IC50 of 39.4  $\mu$ M, a concentration 20 times greater than reported for inhibition of VMAT2 function, suggesting that d-amphetamine interacts with a different site than lobeline on VMAT2 to inhibit monoamine uptake.



These results suggest the use of lobeline and analogs thereof in treating individuals for diseases and pathologies of the **central nervous system**.

IT 90-69-7, Lobeline 552-72-7, Lobelanidine  
579-21-5, Lobelanine

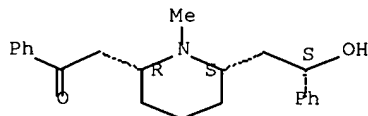
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)  
(lobeline compds. for treatment of **central  
nervous system** disease)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

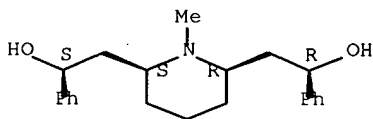
Absolute stereochemistry.



RN 552-72-7 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-,  
( $\alpha R, \alpha' S, 2R, 6S$ )-rel- (9CI) (CA INDEX NAME)

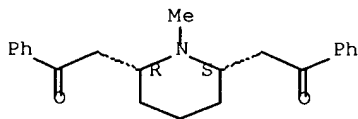
Relative stereochemistry.



RN 579-21-5 HCAPLUS

CN Ethanone, 2,2'-(1-methyl-2,6-piperidinediyl)bis[1-phenyl-,  
(2R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IC ICM A61K031-445

INCL 514317000

CC 1-11 (Pharmacology)

Section cross-reference(s): 63

ST **central nervous system** therapeutic  
lobeline compd

IT Brain, disease

(Gilles de la Tourette syndrome; lobeline compds. for treatment  
of **central nervous system**  
disease)

IT Nervous system

(Huntington's chorea; lobeline compds. for treatment of  
**central nervous system** disease)

IT Mental disorder

- (attention deficit disorder; lobeline compds. for treatment of **central nervous system** disease)
- IT **Nervous system**  
(**central**, disease; lobeline compds. for treatment of **central nervous system** disease)
- IT Sleep  
(disorder; lobeline compds. for treatment of **central nervous system** disease)
- IT Biological transport  
(dopamine uptake; lobeline compds. for treatment of **central nervous system** disease)
- IT Transport proteins  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(dopamine-transporting, presynaptic; lobeline compds. for treatment of **central nervous system** disease)
- IT Drug delivery systems  
(injections, i.m.; lobeline compds. for treatment of **central nervous system** disease)
- IT Drug delivery systems  
(injections, i.v.; lobeline compds. for treatment of **central nervous system** disease)
- IT Drug delivery systems  
(injections, s.c.; lobeline compds. for treatment of **central nervous system** disease)
- IT Antiparkinsonian agents  
Antipsychotics  
Anxiolytics  
Myasthenia gravis  
Nervous system agents  
Nicotinic antagonists  
Schizophrenia  
(lobeline compds. for treatment of **central nervous system** disease)
- IT Nicotinic receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(lobeline compds. for treatment of **central nervous system** disease)
- IT Transport proteins  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(monoamine-transporting, vesicular, including VMAT2; lobeline compds. for treatment of **central nervous system** disease)
- IT Drug delivery systems  
(nasal; lobeline compds. for treatment of **central nervous system** disease)
- IT Mental disorder  
(obsession-compulsion; lobeline compds. for treatment of **central nervous system** disease)
- IT Drug delivery systems  
(oral; lobeline compds. for treatment of **central nervous system** disease)
- IT Anxiety  
(panic disorder; lobeline compds. for treatment of **central nervous system** disease)
- IT Synapse  
(presynapse; lobeline compds. for treatment of **central nervous system** disease)
- IT Mental disorder  
(psychosis; lobeline compds. for treatment of **central nervous system** disease)
- IT Drug delivery systems  
(rectal; lobeline compds. for treatment of **central nervous system** disease)

IT Synapse  
(synaptic vesicle; lobeline compds. for treatment of  
**central nervous system** disease)

IT Synapse  
(synaptosome, striatal; lobeline compds. for treatment of  
**central nervous system** disease)

IT Drug delivery systems  
(transdermal; lobeline compds. for treatment of **central  
nervous system** disease)

IT Brain, disease  
Head  
(trauma; lobeline compds. for treatment of **central  
nervous system** disease)

IT 51-64-9 54-11-5, Nicotine 58-46-8, Tetrabenazine 60-40-2,  
Mecamylamine 555-57-7, Pargyline 3466-75-9,  
Dihydrotetrabenazine 24526-64-5, Nomifensine 67469-78-7, GBR  
12909  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); BIOL (Biological study)  
(lobeline compds. for treatment of **central  
nervous system** disease)

IT 90-69-7, Lobeline 552-72-7, Lobelanidine  
579-21-5, Lobelanine  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); **THU (Therapeutic use)**;  
BIOL (Biological study); USES (Uses)  
(lobeline compds. for treatment of **central  
nervous system** disease)

IT 102-32-9, DOPAC  
RL: BOC (Biological occurrence); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study); OCCU  
(Occurrence); PROC (Process)  
(lobeline compds. for treatment of **central  
nervous system** disease)

IT 7440-70-2, Calcium, biological studies  
RL: BPR (Biological process); BSU (Biological study,  
unclassified); BIOL (Biological study); PROC (Process)  
(lobeline compds. for treatment of **central  
nervous system** disease)

IT 51-61-6, Dopamine, biological studies  
RL: BOC (Biological occurrence); BPR (Biological process); BSU  
(Biological study, unclassified); BIOL (Biological study); OCCU  
(Occurrence); PROC (Process)  
(uptake; lobeline compds. for treatment of **central  
nervous system** disease)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2000:420967 HCAPLUS Full-text  
DOCUMENT NUMBER: 133:48900  
TITLE: Use of apomorphine in the manufacture of a  
medicament for the treatment of organic  
erectile dysfunction in males  
INVENTOR(S): Kling, Karen; Perdok, Renee J.; Ruff, Dustin  
D.  
PATENT ASSIGNEE(S): Abbott Laboratories, USA  
SOURCE: PCT Int. Appl., 23 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

-----  
WO 2000035457      A1      20000622      WO 1999-US29449  
1999  
1213  
<--  
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,  
CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM,  
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
TZ, UA, UG, UZ, VN, YU, ZA, ZW  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN,  
TD, TG  
US 6291471      B1      20010918      US 1998-213567  
1998  
1217  
CA 2354601      AA      20000622      CA 1999-2354601  
1999  
1213  
<--  
EP 1140094      A1      20011010      EP 1999-966147  
1999  
1213  
<--  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT, IE, SI, FI, RO  
TR 200101719      T2      20020821      TR 2001-200101719  
1999  
1213  
<--  
BR 9916114      A      20030114      BR 1999-16114  
1999  
1213  
<--  
JP 2003521462      T2      20030715      JP 2000-587777  
1999  
1213  
<--  
NZ 511790      A      20040430      NZ 1999-511790  
1999  
1213  
<--  
TW 577740      B      20040301      TW 1999-88122257  
2000  
0111  
<--  
ZA 2001004146      A      20020821      ZA 2001-4146  
2001  
0521  
<--  
NO 2001002985      A      20010816      NO 2001-2985  
2001  
0615  
<--  
BG 105664      A      20020228      BG 2001-105664  
2001  
0703  
<--  
PRIORITY APPLN. INFO.:      US 1998-213567      A  
1998  
1217  
<--  
WO 1999-US29449      W  
1999  
1213

&lt;--

AB A method of treating organic erectile dysfunction, particularly vasculogenic erectile dysfunction comprises administering to a male in need of such treatment a therapeutically effective amount of apomorphine or a pharmaceutically acceptable salt or pro-drug thereof. The apomorphine may be coadministered with an antiemetic agent. A sublingual tablet contained apomorphine hydrochloride 5, ascorbic acid 5, mannitol 67.9, Mg stearate 1, nicotine 1,  $\beta$ -cyclodextrin 20, and D&C Yellow aluminum lake 0.1 mg.

IT 134-64-5, Lobeline sulfate

RL: THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(apomorphine and antiemetic combinations for treatment of erectile dysfunctions from cardiovascular disease)

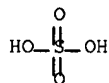
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

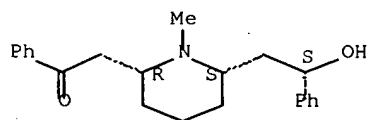


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



IC ICM A61K031-485

ICS A61P015-10; A61K031-485; A61K031-454

CC 63-6 (Pharmaceuticals)

IT 50-53-3, Chlorpromazine, biological studies 51-34-3, Scopolamine 54-11-5, Nicotine 58-00-4, Apomorphine 58-38-8, Prochlorperazine 84-04-8, Pipamazine 129-74-8, Buclizine hydrochloride 134-64-5, Lobeline sulfate 138-56-7, Trimethobenzamide 303-25-3, Cyclizine hydrochloride 314-19-2, Apomorphine hydrochloride 364-62-5, Metoclopramide 523-87-5, Dimenhydrinate 1420-55-9, Thiethylperazine 14008-44-7, Metopimazine 17297-82-4 57808-66-9, Domperidone 99614-02-5, Ondansetron

RL: THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(apomorphine and antiemetic combinations for treatment of erectile dysfunctions from cardiovascular disease)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1999:819232 HCAPLUS Full-text  
 DOCUMENT NUMBER: 132:54897  
 TITLE: Apomorphine-containing dosage forms for  
 ameliorating male erectile dysfunction  
 INVENTOR(S): El-Rashidy, Ragab; Ronsen, Bruce  
 PATENT ASSIGNEE(S): Pentech Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 75 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9966916	A1	19991229	WO 1999-US14053	1999 0622
<--				
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6121276	A	20000919	US 1998-102406	1998 0622
<--				
CA 2336095	AA	19991229	CA 1999-2336095	1999 0622
<--				
AU 9947058	A1	20000110	AU 1999-47058	1999 0622
<--				
AU 776686	B2	20040916		
EP 1094799	A1	20010502	EP 1999-930538	1999 0622
<--				
EP 1094799	B1	20060816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
BR 9911408	A	20011204	BR 1999-11408	1999 0622
<--				
JP 2002518439	T2	20020625	JP 2000-555602	1999 0622
<--				
NZ 509438	A	20030630	NZ 1999-509438	1999 0622
<--				
NO 2000006560	A	20010222	NO 2000-6560	2000 1221
<--				

10/813,647

HK 1040179

A1

20060106

HK 2001-109138

2002  
0325

PRIORITY APPLN. INFO.:

<--  
US 1998-102406

A  
1998  
0622

<--  
US 1994-231250

B2  
1994  
0422

<--  
US 1995-546498

A2  
1995  
1020

<--  
WO 1999-US14053

W  
1999  
0622

AB Psychogenic impotence can be ameliorated without substantial undesirable side effects by administration of apomorphine (I) and an antiemetic agent in an amount sufficient to substantially reduce nausea symptoms associated with the use of apomorphine. Extensive pharmacol. data are given showing the effectiveness of I. A formulation was given for a I-nicotine combination tablet.

IT 134-64-5

RL: MOA (Modifier or additive use); THU (Therapeutic use)  
; BIOL (Biological study); USES (Uses)  
(apomorphine-containing dosage forms for ameliorating male erectile dysfunction)

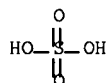
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidiny]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

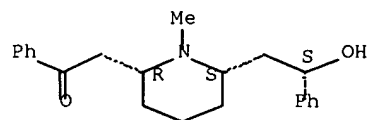


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

10/813,647

IT 51-34-3 54-11-5 58-38-8 60-90-2 68-88-2 134-64-5  
523-87-5 569-65-3 3254-89-5 6505-86-8 7232-21-5  
14008-44-7

RL: MOA (Modifier or additive use); THU (Therapeutic use)

; BIOL (Biological study); USES (Uses)

(apomorphine-containing dosage forms for ameliorating male erectile dysfunction)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:613666 HCAPLUS Full-text

DOCUMENT NUMBER: 131:223511

TITLE: Combination of a GABA-A alpha 5 inverse  
agonist and a nicotinic agonist for treating  
neurodegenerative conditions

INVENTOR(S): Dawson, Gerard Raphael

PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947142	A1	19990923	WO 1999-GB800	1999 0316
<--				
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2324237	AA	19990923	CA 1999-2324237	1999 0316
<--				
AU 9928477	A1	19991011	AU 1999-28477	1999 0316
<--				
AU 752013	B2	20020905		
EP 1061925	A1	20001227	EP 1999-909110	1999 0316
<--				
EP 1061925	B1	20021030		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002506822	T2	20020305	JP 2000-536382	1999 0316
<--				
AT 226823	E	20021115	AT 1999-909110	1999 0316
<--				
ES 2185321	T3	20030416	ES 1999-909110	



1999  
0316

PRIORITY APPLN. INFO.:

<--  
GB 1998-5559

A

1998  
0316<--  
WO 1999-GB800

W

1999  
0316

AB The present invention relates to a combination of a nicotinic agonist and an inverse agonist of the GABAA  $\alpha 5$  receptor subtype, used sep., sequentially or simultaneously, in treating neurodegenerative conditions such as Alzheimer's disease and parkinsonism. Suitable GABA-A  $\alpha 5$  inverse agonists are derivs. of 1,2,4-triazolo[3,4-a]phthalazine and nicotinic agonists are selected from nicotine, lobeline, tetramethylammonium, 1,1-dimethyl-4-phenylpyrazinium, and ABT 418. A suitable dosage level is .apprx. 0.01-5 mg/kg per day of each active ingredient administered 1-4 times per day.

IT 90-69-7, Lobeline

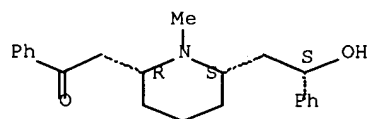
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**;  
BIOL (Biological study); USES (Uses)

(combination of GABA-A  $\alpha 5$  inverse agonist and nicotinic agonist for treating neurodegenerative disorders)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-50

ICS A61K031-495; A61K031-465; A61K031-445; A61K031-42; A61K031-14

CC 1-11 (Pharmacology)

Section cross-reference(s): 63

IT 51-92-3, Tetramethylammonium 54-11-5 90-69-7, Lobeline

147402-53-7, ABT 418 215873-94-2 215874-86-5 244082-04-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**;  
BIOL (Biological study); USES (Uses)

(combination of GABA-A  $\alpha 5$  inverse agonist and nicotinic agonist for treating neurodegenerative disorders)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:510839 HCAPLUS Full-text

DOCUMENT NUMBER: 131:281005

TITLE: Lobeline: Structure-Affinity Investigation of  
Nicotinic Acetylcholinergic Receptor Binding  
AUTHOR(S): Flammia, Dwight; Dukat, Malgorzata; Damaj, M.  
Imad; Martin, Billy; Glennon, Richard A.

CORPORATE SOURCE: Department of Medicinal Chemistry School of  
Pharmacy and Department of Pharmacology and  
Toxicology School of Medicine, Virginia  
Commonwealth University, Richmond, VA,  
23298-0540, USA

SOURCE: Journal of Medicinal Chemistry (1999)  
 ), 42(18), 3726-3731  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB (-)Lobeline (1) and (-)nicotine (2) bind at neuronal nicotinic cholinergic (nACh) receptors with high affinity ( $K_i = 4$  and  $2$  nM, resp.). Previous attempts to determine whether lobeline fits the currently accepted nicotinic pharmacophore model have led to suggestions that the carbonyl function, rather than the hydroxyl group, is a major contributor to binding. Interestingly, however, it has never been empirically demonstrated that either oxygen function is actually required for interaction with the receptor. In the present investigation we systematically examined a number of abbreviated analogs of lobeline and found that removal of either one or both oxygen functions reduces the affinity of lobeline by at least 25-fold; furthermore, oxidation of the (-)lobeline hydroxyl group (to afford lobelanine) or reduction of the carbonyl group (to afford lobelanidine) also resulted in decreased affinity. Although it is likely that both oxygen functions contribute to the high affinity of (-)lobeline at nACh receptors, it is concluded that the presence of both oxygen functions is not a requirement for binding; i.e., replacement of the (-)lobeline hydroxyl group with a chloro group had no effect on affinity. Another finding of the present investigation is that removal of either one or both oxygen functions of lobeline results in compds. that retain the analgesic activity and potency of (-)lobeline, indicating that there is no direct relationship between neuronal nicotinic cholinergic (primarily  $\alpha 4 \beta 2$  type) receptor affinity and spinal analgesia as measured in the tail-flick assay.

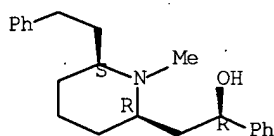
IT 246178-14-3P 246178-16-5P 246178-17-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (lobeline analogs: structure-affinity investigation of neuronal nicotinic receptor binding)

RN 246178-14-3 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-, hydrochloride, ( $\alpha R, 2R, 6S$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+)...



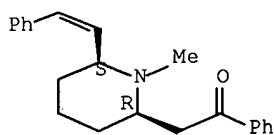
● HCl

RN 246178-16-5 HCAPLUS

CN Ethanone, 2-[(2R,6S)-1-methyl-6-(2-phenylethenyl)-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

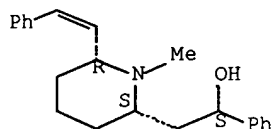


RN 246178-17-6 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethenyl)-,  
( $\alpha$ S,2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



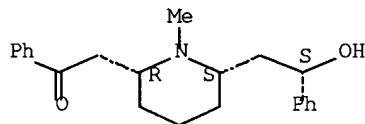
IT 134-63-4, (-)-Lobeline hydrochloride

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); PRP (Properties); RCT  
(Reactant); THU (Therapeutic use); BIOL (Biological  
study); RACT (Reactant or reagent); USES (Uses)  
(lobeline analogs: structure-affinity investigation of neuronal  
nicotinic receptor binding)

RN 134-63-4 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-  
piperidinyl]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

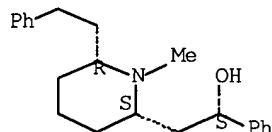
IT 246178-15-4P 246178-18-7P

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); PRP (Properties); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(lobeline analogs: structure-affinity investigation of neuronal  
nicotinic receptor binding)

RN 246178-15-4 HCAPLUS

CN 2-Piperidineethanol, 1-methyl- $\alpha$ -phenyl-6-(2-phenylethyl)-,  
hydrochloride, ( $\alpha$ S,2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

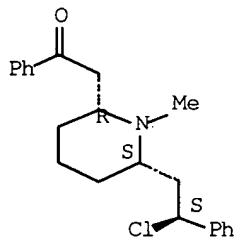


● HCl

RN 246178-18-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-chloro-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

IT 6112-86-3, Lobelanidine, hydrochloride 6168-88-3

, Lobelanine, hydrochloride 246178-19-8

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); PRP (Properties); THU

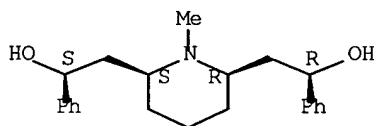
(Therapeutic use); BIOL (Biological study); USES (Uses)

(lobeline analogs: structure-affinity investigation of neuronal nicotinic receptor binding)

RN 6112-86-3 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-, hydrochloride, ( $\alpha R,\alpha'S,2R,6S$ )-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

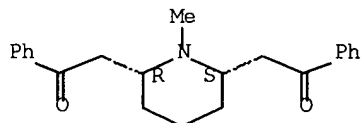


● HCl

RN 6168-88-3 HCAPLUS

CN Ethanone, 2,2'-[(2R,6S)-1-methyl-2,6-piperidinediyl]bis[1-phenyl-, hydrochloride, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

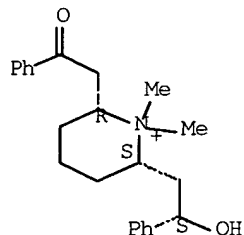


● HCl

RN 246178-19-8 HCAPLUS

CN Piperidinium, 2-[(2S)-2-hydroxy-2-phenylethyl]-1,1-dimethyl-6-(2-oxo-2-phenylethyl)-, iodide, (2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

● I<sup>-</sup>

CC 1-3 (Pharmacology)

IT 246178-14-3P 246178-16-5P 246178-17-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (lobeline analogs: structure-affinity investigation of neuronal nicotinic receptor binding)

IT 134-63-4, (-)-Lobeline hydrochloride

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
 (lobeline analogs: structure-affinity investigation of neuronal nicotinic receptor binding)

IT 246178-15-4P 246178-18-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (lobeline analogs: structure-affinity investigation of neuronal nicotinic receptor binding)

IT 54-11-5 879-72-1 2298-49-9 5424-50-0 **6112-86-3**, Lobelanidine, hydrochloride **6168-88-3**, Lobelanine, hydrochloride 211369-50-5 246178-08-5 246178-10-9 246178-11-0 246178-12-1 **246178-19-8** 246244-18-8 246244-19-9, Lobelan hydrochloride

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)  
 (lobeline analogs: structure-affinity investigation of neuronal nicotinic receptor binding)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:719138 HCAPLUS Full-text

DOCUMENT NUMBER: 129:326105

TITLE: Lobeline compounds as a treatment for

10/813,647

psychostimulant abuse and withdrawal, and for  
**eating disorders**  
 INVENTOR(S): Crooks, Peter A.; Dwoskin, Linda P.  
 PATENT ASSIGNEE(S): University of Kentucky Research Foundation,  
 USA  
 SOURCE: U.S., 20 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5830904	A	19981103	US 1997-795852	1997 0205
US 6087376	A	20000711	US 1998-89420	1998 0603
PRIORITY APPLN. INFO.: US 1997-795852 A2 1997 0205				

OTHER SOURCE(S): MARPAT 129:326105

AB Methods are disclosed that suggest the use of lobeline and analogs thereof in **treating** individuals for **drug** dependence and withdrawal and for **eating disorders**. Lobeline evoked [3H]overflow from rat striatal slices preloaded with [3H]DA (3,4-dihydroxyphenylethyl-2-[N-3H]- amine), in a concentration-dependent, calcium-independent and mecamylamine-insensitive manner. A lobeline-induced inhibition of synaptic vesicular DA transport and subsequent redistribution of presynaptic DA storage may be the mechanism by which lobeline evokes DA release. Clearly, lobeline evokes DA release by a mechanism different from that of nicotine, which may explain the reported differences in the behavioral effects of these drugs, and the differences in their abilities to upregulated nicotinic receptors following chronic administration.

IT 90-69-7, Lobeline 90-69-7D, Lobeline, pharmaceutically-acceptable salts 552-72-7, Lobelanidine 552-72-7D, Lobelanidine, pharmaceutically-acceptable salts 579-21-5

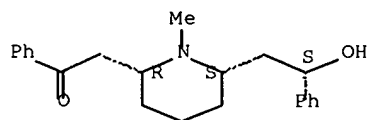
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

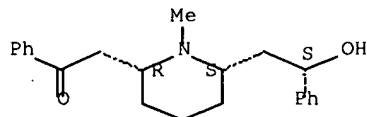
Absolute stereochemistry.



RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

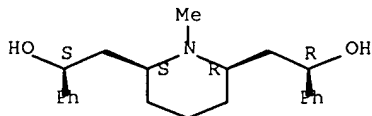
Absolute stereochemistry.



RN 552-72-7 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-,  
( $\alpha R,\alpha'S,2R,6S$ )-rel- (9CI) (CA INDEX NAME)

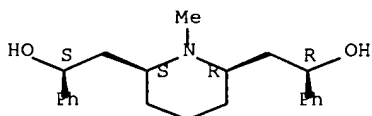
Relative stereochemistry.



RN 552-72-7 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-,  
( $\alpha R,\alpha'S,2R,6S$ )-rel- (9CI) (CA INDEX NAME)

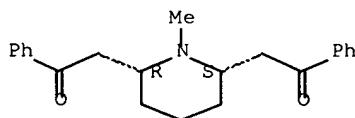
Relative stereochemistry.



RN 579-21-5 HCAPLUS

CN Ethanone, 2,2'-(1-methyl-2,6-piperidinediyl)bis[1-phenyl-,  
(2R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IC ICM A61K031-445

INCL 514317000

CC 1-11 (Pharmacology)

ST lobeline treatment psychostimulant abuse withdrawal;  
**eating disorder** treatment lobeline

IT Psychotomimetics

(as **drug of abuse**; lobeline compds. as a  
treatment for psychostimulant abuse and withdrawal, and for  
**eating disorders**)

IT Cannabinoids

Opioids

RL: ADV (Adverse effect, including toxicity); BIOL (Biological  
study)

(as **drug of abuse**; lobeline compds. as a

- treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT **Nervous system**  
(**central**, dopamine release and uptake by cells of, lobeline effect on; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT **Appetite**  
(disorder; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT **Drug dependence**  
**Drug withdrawal**  
**Obesity**  
(lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT **Nicotinic receptors**  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(lobeline effect on; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT **Synapse**  
(synaptic vesicle, lobeline effects on, of rat; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT **Synapse**  
(synaptosome, lobeline effects on, of rat; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT 50-36-2, Cocaine 58-08-2, Caffeine, biological studies  
64-17-5, Ethanol, biological studies 77-10-1, Phencyclidine  
300-62-9D, Amphetamine, compds.  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(as **drug of abuse**; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT 67-52-7D, 2,4,6(1H,3H,5H)-Pyrimidinetrione, derivs. 12794-10-4D, Benzodiazepine, derivs.  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as **drug of abuse**; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT 90-69-7, Lobeline 90-69-7D, Lobeline, pharmaceutically-acceptable salts 552-72-7, Lobelanidine 552-72-7D, Lobelanidine, pharmaceutically-acceptable salts 579-21-5  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT 54-11-5, Nicotine  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(lobeline effect compared to; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)
- IT 51-61-6, Dopamine, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)  
(release and uptake of, by cells of **central nervous system**, lobeline effect on; lobeline compds. as a treatment for psychostimulant abuse and withdrawal, and for **eating disorders**)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE



10/813,647

FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1998:548534 HCAPLUS Full-text  
 DOCUMENT NUMBER: 129:171769  
 TITLE: Pharmaceutical composition for treatment of  
 synaptic dysfunction comprising an oxime  
 INVENTOR(S): Viner, Norman M.  
 PATENT ASSIGNEE(S): Synapse Pharmaceuticals International, Inc.,  
 Can.  
 SOURCE: PCT Int. Appl., 55 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
WO 9834615	A1	19980813	WO 1998-CA94	1998 0205
<--				
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6166032	A	20001226	US 1997-797251	1997 0207
US 5900418	A	19990504	US 1997-795247	1997 0210
<--				
US 5981549	A	19991109	US 1997-801802	1997 0214
<--				
US 5760049	A	19980602	US 1997-803723	1997 0221
<--				
US 5824684	A	19981020	US 1997-803722	1997 0221
<--				
US 5902816	A	19990511	US 1997-803721	1997 0221
<--				
US 5916903	A	19990629	US 1997-807273	1997 0228
<--				
CA 2279531	AA	19980813	CA 1998-2279531	1998 0205
<--				
ZA 9800960	A	19980817	ZA 1998-960	

				1998 0205
			<--	
AU 9859775	A1	19980826	AU 1998-59775	
				1998 0205
			<--	
EP 1014981	A1	20000705	EP 1998-902893	
				1998 0205
			<--	
			R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI	
JP 2001511159	T2	20010807	JP 1998-533466	
				1998 0205
			<--	
PRIORITY APPLN. INFO.:			US 1997-797251	A2
				1997 0207
			<--	
			US 1997-795247	A2
				1997 0210
			<--	
			US 1997-801801	A2
				1997 0214
			<--	
			US 1997-801802	A2
				1997 0214
			<--	
			US 1997-803719	A2
				1997 0221
			<--	
			US 1997-803721	A2
				1997 0221
			<--	
			US 1997-803722	A2
				1997 0221
			<--	
			US 1997-803723	A2
				1997 0221
			<--	
			US 1997-807273	A2
				1997 0228
			<--	
			WO 1998-CA94	W
				1998 0205
			<--	

## OTHER SOURCE(S): MARPAT 129:171769

AB A pharmaceutical composition is provided for treatment of chronic symptoms of synaptic dysfunction and related disease disorders comprising an effective amount of a pharmaceutically acceptable oxime which is physiologically active such as an acetylcholine esterase reactivator optionally in association with an additional pharmacologically active agent. The pharmaceutical composition has wide-ranging applicability in the treatment of withdrawal symptoms due to the cessation of tobacco use, respiratory disease, drug and alcohol addiction, disorders of the central and peripheral nervous systems, treatment of antineoplastic disease as well as the reduction of adverse effects of antineoplastic disease treatment, cardiac disorders and circulatory disease, obesity, fatigue

syndromes, endocrine and immune system disorders, dysfunction of gastrointestinal motility and irritable bowel syndrome, and heavy metal poisoning.

IT 90-69-7, Lobeline

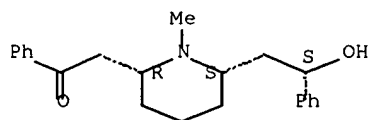
RL: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(stimulant; pharmaceutical composition for treatment of synaptic dysfunction comprising oxime)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-46

ICS A61K031-46; A61K031-44

CC 4-8 (Toxicology)

Section cross-reference(s): 1, 63

IT 59-26-7, Nikethamide 63-75-2, Arecoline 90-69-7,  
Lobeline 92-13-7, Pilocarpine 300-54-9, Muscarine 304-84-7,  
Ethamivan 486-56-6, Cotinine 674-38-4, Bethanechol

RL: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(stimulant; pharmaceutical composition for treatment of synaptic dysfunction comprising oxime)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L51 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:478949 HCAPLUS Full-text

DOCUMENT NUMBER: 129:117865

TITLE: Methods and articles of manufacture for  
treating nicotine withdrawal symptoms, for  
nicotine cessation, and for monitoring  
nicotine use

INVENTOR(S): Eswara, Amruta R.; Muni, Neal; Schneider, F.  
Howard; Mione, Peter J.

PATENT ASSIGNEE(S): DynaGen, Inc., USA

SOURCE: U.S., 23 pp., Cont.-in-part of U.S. Ser. No.  
487,853, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	
US 5780051	A	19980714	US 1997-779281	1997 0122
US 5403595	A	19950404	US 1993-135847	1993 1013
US 5414005	A	19950509	US 1993-145203	

A

<--

1995  
0403

←--

B3

1992  
0402

←--

A2

1992  
0507

<---

A3

1993  
1013

←--

B3

1993  
1015

<--

A3

1993  
1028

<--

A3

1994  
0725

<---

A3

1995  
0403

<--

B2

1995  
0607

←--

B2

1991  
0507

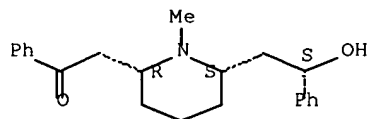
<--

IT 90-69-7, Lobeline 90-69-7D, Lobeline, analogs  
134-64-5, Lobeline sulfate

BIOL (Biological study); USES (Uses)

RN 90-69-7 HCAPLUS

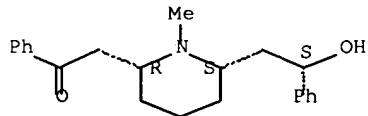
Absolute stereochemistry.



RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



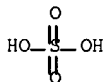
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

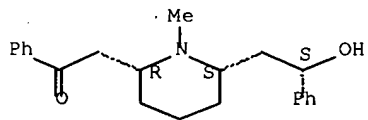


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



IC ICM A61K009-70

ICS A61K009-48; A61K009-50; A61F002-02

INCL 424449000

CC 1-12 (Pharmacology)

Section cross-reference(s): 4

IT 63-75-2, Arecoline 63-75-2D, Arecoline, analogs 90-69-7

, Lobeline 90-69-7D, Lobeline, analogs 134-64-5

, Lobeline sulfate 494-52-0, Anabesine 494-52-0D, Anabesine,

analog 923-32-0, Cystine 923-32-0D, Cystine, analogs

115713-16-1, Isoarecolone 115713-16-1D, Isoarecolone, analogs  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (methods and articles of manufacture for treating nicotine  
 withdrawal symptoms, for nicotine cessation, and for monitoring  
 nicotine use)

REFERENCE COUNT: 125 THERE ARE 125 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L51 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:199587 HCAPLUS Full-text

DOCUMENT NUMBER: 126:272209

TITLE: Lobeline and nicotine evoke [3H]overflow from  
 rat striatal slices preloaded with  
 [3H]dopamine: differential inhibition of  
 synaptosomal and vesicular [3H]dopamine uptake

AUTHOR(S): Teng, Lihong; Crooks, Peter A.; Sonsalla,  
 Patricia K.; Dwoskin, Linda P.

CORPORATE SOURCE: College of Pharmacy and Graduate Center for  
 Toxicology, University of Kentucky, Lexington,  
 KY, USA

SOURCE: Journal of Pharmacology and Experimental  
 Therapeutics (1997), 280(3),  
 1432-1444

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lobeline is currently being developed as a substitution therapy for tobacco smoking  
 cessation. Activation of CNS dopamine (DA) systems results in the reinforcing  
 properties of nicotine. The present study compared the effects of lobeline and  
 nicotine on rat striatum. Both lobeline and nicotine evoked [3H]overflow from striatal  
 slices superfused in the presence of pargyline and nomifensine in the buffer. Marked  
 DA depletion (42-67%) and a concomitant 2-fold increase in dihydroxyphenylacetic acid  
 (DOPAC) in slices superfused with high concns. (30-100  $\mu$ M) of lobeline were observed  
 The effect of nicotine (10  $\mu$ M) was inhibited in a concentration-dependent manner by  
 mecamylamine (1-100  $\mu$ M). However, lobeline (0.1-100  $\mu$ M)-evoked [3H]overflow was  
 calcium-independent, and was not antagonized by mecamylamine (1-100  $\mu$ M), suggesting a  
 mechanism of action other than stimulation of nicotinic receptors. Lobeline inhibited  
 [3H]DA uptake into synaptosomes ( $IC_{50} = 80 \pm 12 \mu$ M) and vesicles ( $IC_{50} = 0.88 \pm 0.001$   
 $\mu$ M), whereas nicotine ( $\leq 100 \mu$ M) did not inhibit synaptosomal or vesicular [3H]DA  
 uptake. In the absence of pargyline and nomifensine in the buffer, endogenous DA was  
 detected in superfusate only in those slices exposed to the highest concentration (100  
 $\mu$ M) of lobeline. However, endogenous DOPAC concentration was increased in a  
 concentration-dependent manner, indicating that lobeline exposure resulted in increased  
 cytosolic DA which was rapidly metabolized to DOPAC. Under these conditions, lobeline  
 (10-100  $\mu$ M) also significantly metabolized (66-85%) DA content; however, no change in  
 DOPAC content was observed The results suggest that, unlike nicotine, lobeline  
 increases DA release by potent inhibition of DA uptake into synaptic vesicles, and a  
 subsequent alteration in presynaptic DA storage.

IT 90-69-7, Lobeline

RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); THU (Therapeutic use);

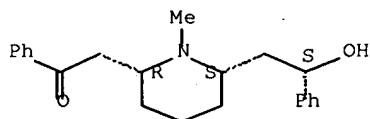
BIOL (Biological study); USES (Uses)

(lobeline and nicotine evoke [3H]overflow from striatal slices  
 preloaded with [3H]dopamine)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-  
 piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-11 (**Pharmacology**)

Section cross-reference(s): 4

IT **90-69-7**, Lobeline

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); **THU (Therapeutic use)**;

BIOL (Biological study); USES (Uses)

(lobeline and nicotine evoke [3H]overflow from striatal slices  
preloaded with [3H]dopamine)

L51 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:708661 HCAPLUS Full-text

DOCUMENT NUMBER: 126:1015

TITLE: Clinical experience with lobeline as a smoking  
cessation agent

AUTHOR(S): Schneider, F. Howard; Olsson, Theodore A.

CORPORATE SOURCE: DynaGen, Inc., Cambridge, MA, 02139, USA

SOURCE: Medicinal Chemistry Research (1996),

6(7/8), 562-570

CODEN: MCREEB; ISSN: 1054-2523

PUBLISHER: Birkhaeuser

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sublingual tablets containing 7.5 mg of lobeline sulfate, recommended to be taken nine times per day for six weeks, resulted in a smoking cessation rate, during the last four weeks of the study, of 29%, compared to the placebo quit rate of 17% (p = .28). This dosage schedule was selected from a short-term study in which the reduction of tobacco withdrawal symptoms by 2.5, 5.0 and 7.5 mg lobeline sulfate sublingual tablets taken 3, 6, 9 or 12 times per day was evaluated. The dosing frequency of nine per day is consistent with blood and brain T<sub>1/2</sub> values of 30-40 min in rats.

IT **90-69-7**, Lobeline

RL: BAC (Biological activity or effector, except adverse); BOC

(Biological occurrence); BSU (Biological study, unclassified);

**THU (Therapeutic use)**; BIOL (Biological study); OCCU

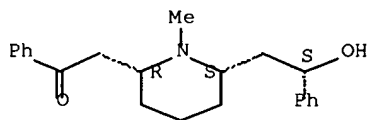
(Occurrence); USES (Uses)

(lobeline sublingual tablets for smoking cessation)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **134-64-5**, Lobeline sulfate

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES

(Uses)

(lobeline sublingual tablets for smoking cessation)

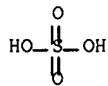
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

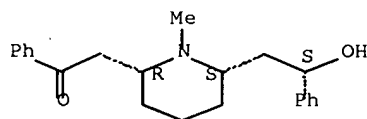


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.

CC 1-11 (**Pharmacology**)

Section cross-reference(s): 4, 63

IT 90-69-7, Lobeline

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (**Therapeutic use**); BIOL (Biological study); OCCU (Occurrence); USES (Uses)

(lobeline sublingual tablets for smoking cessation)

IT 134-64-5, Lobeline sulfate

RL: THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)

(lobeline sublingual tablets for smoking cessation)

L51 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:310352 HCAPLUS Full-text

DOCUMENT NUMBER: 125:1220

TITLE: Effects of stimulation or blockade of central nicotinic-cholinergic receptors on performance of a novel version of the rat stimulus discrimination task

AUTHOR(S): Terry, A. V., Jr.; Buccafusco, J. J.; Jackson, W. J.; Zagrodnik, S.; Evans-Martin, F. F.; Decker, M. W.

CORPORATE SOURCE: Univ. of Georgia Clinical Pharmacy Program, Medical College of Georgia, Augusta, GA, 30912-2390, USA

SOURCE: Psychopharmacology (Berlin) (1996), 123(2), 172-181

CODEN: PSCHDL; ISSN: 0033-3158

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study evaluated the effects of two central nicotinic-cholinergic receptor agonists and an antagonist on performance accuracy of a rat, delayed stimulus discrimination task (DSDT). Rats were trained to discriminate between an auditory and visual stimulus by pressing a right or left lever. To diminish the rat's ability to use mediating spatial strategies to solve the task, computer automated, retractable doors separated



the animal from the levers during delay intervals, thus reducing positioning at the lever. After stable baselines were achieved, rats were grouped and administered placebo (saline) and nicotine, lobeline or mecamylamine in a randomized dose series. Each group received two complete series of the selected compound on different occasions. Mecamylamine impaired DSDT accuracy in a dose-dependent manner while optimal doses of nicotine and lobeline significantly improved accuracy. Nicotine differed from lobeline in regard to its interaction with a dose of mecamylamine (1.0 mg/kg) that had not impaired DSDT accuracy. Combined administration of lobeline and mecamylamine was followed by a significantly increased level of DSDT accuracy that was similar to the improvement following administration of lobeline alone. In contrast, combined administration of nicotine and mecamylamine did not result in increased DSDT accuracy. Furthermore, lobeline administration similarly improved accuracy of trials associated with both the light and the tone, while nicotine improved accuracy of trials associated with the light to a much greater degree. These data suggest that the increases in DSDT accuracy associated with lobeline may be expressed through non-nicotinic mechanisms or a nicotinic receptor which is not blocked by mecamylamine.

IT 90-69-7, Lobeline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use);

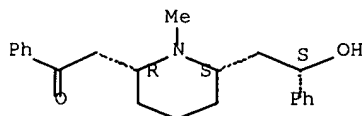
BIOL (Biological study); USES (Uses)

(effects of stimulation or blockade of central nicotinic-cholinergic receptors on performance of a novel version of rat stimulus discrimination task)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-11 (Pharmacology)

IT 54-11-5, Nicotine 90-69-7, Lobeline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(effects of stimulation or blockade of central nicotinic-cholinergic receptors on performance of a novel version of rat stimulus discrimination task)

L51 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:662837 HCAPLUS Full-text

DOCUMENT NUMBER: 123:40991

TITLE: Use of nicotine substitutes for the treatment of nicotine withdrawal

INVENTOR(S): Schneider, F. Howard; Muni, Indu A.; Murty, B. Ram; Pandya, Mahendra K.; Matharu, Rajinder P. S.

PATENT ASSIGNEE(S): Dynagen, Inc., USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511678	A1	19950504	WO 1994-US12441	

1994

1028

&lt;--

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP,  
 KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL,  
 RO, RU, SI, SK, TJ, TT, UA, US, US, UZ, VN

RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,  
 IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,  
 ML, MR, NE, SN, TD, TG

US 5414005 A 19950509 US 1993-145203

1993

1028

&lt;--

AU 9480960 A1 19950522 AU 1994-80960

1994

1028

&lt;--

PRIORITY APPLN. INFO.: US 1993-144309 A

1993

1028

&lt;--

US 1993-145203 A

1993

1028

&lt;--

WO 1994-US12441 W

1994

1028

&lt;--

AB The present application features methods and articles for alleviating acute symptoms of nicotine withdrawal and as an aid in smoking cessation. The invention features lobeline and its salts held in sublingual tablets, and liquid preps. for administration to the sublingual and nasal mucosa and pulmonary tissues and a powder for administering to the pulmonary tissues. A sublingual tablet containing 2.5 mg lobeline was formulated and its effect was clin. tested among smokers.

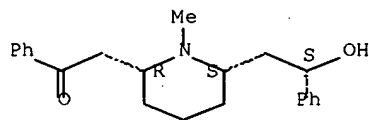
IT 90-69-7, Lobeline 134-63-4, Lobeline hydrochloride 134-64-5, Lobeline sulfate  
 RL: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)

(lobeline as nicotine substitutes for treatment of nicotine withdrawal symptoms)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

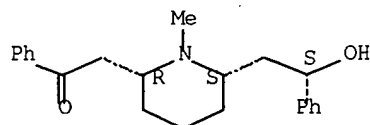
Absolute stereochemistry.



RN 134-63-4 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

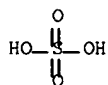


● HCl

RN 134-64-5 HCAPLUS  
 CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

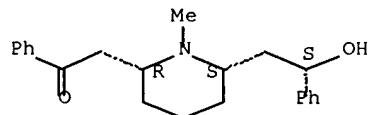
CRN 7664-93-9  
 CMF H2 O4 S



CM 2

CRN 90-69-7  
 CMF C22 H27 N O2

Absolute stereochemistry.



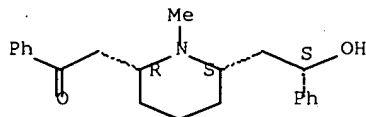
IC ICM A61K031-445  
 ICS A61K031-455; A61K031-44  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1  
 IT 90-69-7, Lobeline 134-63-4, Lobeline hydrochloride 134-64-5, Lobeline sulfate  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (lobeline as nicotine substitutes for treatment of nicotine withdrawal symptoms)

L51 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:662836 HCAPLUS Full-text  
 DOCUMENT NUMBER: 123:40990  
 TITLE: Use of lobeline for the treatment of nicotine withdrawal symptoms  
 INVENTOR(S): Schneider, F. Howard; Muni, Indu A.; Murty, B. Ram; Pandya, Mahendra K.; Matharu, Rajinder P. S.  
 PATENT ASSIGNEE(S): Dynagen, Inc., USA

SOURCE: PCT Int. Appl., 31 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511679	A1	19950504	WO 1994-US12442	1994 1028
<--				
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5414005	A	19950509	US 1993-145203	1993 1028
<--				
AU 9510456	A1	19950522	AU 1995-10456	1994 1028
<--				
EP 725640	A1	19960814	EP 1995-901081	1994 1028
<--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09507053	T2	19970715	JP 1994-512876	1994 1028
<--				
PRIORITY APPLN. INFO.:			US 1993-144309	A 1993 1028
<--				
			US 1993-145203	A 1993 1028
<--				
			WO 1994-US12442	W 1994 1028
<--				
AB	The present application features methods and articles for alleviating acute symptoms of nicotine withdrawal and as an aid in smoking cessation. The invention features lobeline held in sublingual tablets. For example, a sublingual tablet containing 2.5 mg lobeline sulfate was formulated and its effects were clin. tested among smokers.			
IT	90-69-7, Lobeline 134-63-4, Lobeline hydrochloride 134-64-5, Lobeline sulfate			
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(lobeline for treatment of nicotine withdrawal symptoms)			
RN	90-69-7 HCAPLUS			
CN	Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)			

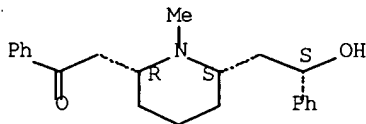
Absolute stereochemistry.



RN 134-63-4 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

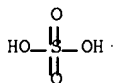
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

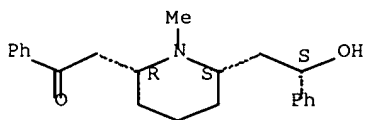


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



IC ICM A61K031-445

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT 90-69-7, Lobeline 134-63-4, Lobeline hydrochloride 134-64-5, Lobeline sulfate

10/813,647

RL: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(lobeline for treatment of nicotine withdrawal symptoms)

L51 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1995:602400 HCAPLUS Full-text  
DOCUMENT NUMBER: 123:17917  
TITLE: Lobeline and its analogs for the treatment of  
nicotine withdrawal and as an aid in smoking  
cessation  
INVENTOR(S): Schneider, F. Howard; Muni, Indu A.; Murty, B.  
Ram; Pandya, Mahendra K.; Matharu, Rajinder P.  
S.  
PATENT ASSIGNEE(S): DynaGen, Inc., USA  
SOURCE: U.S., 6 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 7  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5414005	A	19950509	US 1993-145203	1993 1028
CA 2174747	AA	19950504	CA 1994-2174747	1994 1028
WO 9511678	A1	19950504	WO 1994-US12441	1994 1028
WO 9511679	A1	19950504	WO 1994-US12442	1994 1028
AU 9480960	A1	19950522	AU 1994-80960	1994 1028
AU 9510456	A1	19950522	AU 1995-10456	1994 1028
EP 725640	A1	19960814	EP 1995-901081	1994 1028
JP 09507053	T2	19970715	JP 1994-512876	

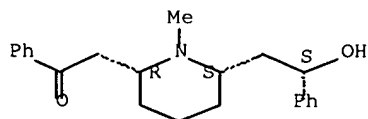
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, US, UZ, VN  
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, US, UZ, VN  
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

				1994
				1028
			<--	
US 5780051	A	19980714	US 1997-779281	
				1997
				0122
			<--	
PRIORITY APPLN. INFO.:			US 1992-862051	B3
				1992
				0402
			<--	
			US 1992-881740	A2
				1992
				0507
			<--	
			US 1993-135847	A3
				1993
				1013
			<--	
			US 1993-137687	B3
				1993
				1015
			<--	
			US 1993-144309	A
				1993
				1028
			<--	
			US 1993-145203	A
				1993
				1028
			<--	
			US 1994-279619	A3
				1994
				0725
			<--	
			WO 1994-US12441	W
				1994
				1028
			<--	
			WO 1994-US12442	W
				1994
				1028
			<--	
			US 1995-415859	A3
				1995
				0403
			<--	
			US 1995-487853	B2
				1995
				0607
			<--	
AB	Sublingual tablets comprise lobeline, its analogs, or salts with disintegrants capable of causing disintegration within a 5 min period in the presence of oral secretions for alleviating acute symptoms of nicotine withdrawal and as an aid in smoking cessation. A sublingual tablet contained lobeline sulfate 2.5, mannitol 31.5, microcryst. cellulose 40.35, Na starch glycolate 2.6, Na saccharin 0.5, peppermint flavors 0.75, Magnasweet 0.5, vanilla flavor 0.2, D&C Yellow Number 10 0.2, Mg stearate 0.5, and Aerosil-200 0.4 mg.			
IT	90-69-7, Lobeline 134-63-4, Lobeline hydrochloride 134-64-5, Lobeline sulfate			
	RL: THU (Therapeutic use); BIOL (Biological study); USES			
	(Uses)			
	(sublingual tablets containing lobeline for treatment of nicotine withdrawal and as aid in smoking cessation)			
RN	90-69-7 HCAPLUS			
CN	Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)			

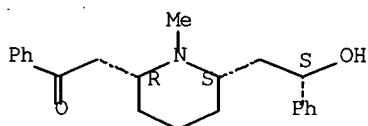
Absolute stereochemistry.



RN 134-63-4 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

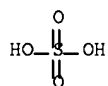
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

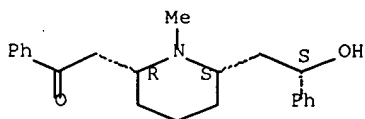


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



IC ICM A61K009-20

ICS A61K031-465



INCL 514343000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 4

IT 90-69-7, Lobeline 134-63-4, Lobeline  
hydrochloride 134-64-5, Lobeline sulfateRL: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)(sublingual tablets containing lobeline for treatment of nicotine  
withdrawal and as aid in smoking cessation)

L51 ANSWER 27 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:221528 HCAPLUS Full-text

DOCUMENT NUMBER: 122:305842

TITLE: Reversal of multidrug resistance by  
bis(phenylalkyl)amines and structurally  
related compounds

AUTHOR(S): Ramu, Avner; Ramu, Nili

CORPORATE SOURCE: Department Oncology, Hadassah University  
Hospital, Jerusalem, 91120, Israel

SOURCE: Cancer Chemotherapy and Pharmacology (1994), 34(5), 423-30

CODEN: CCPHDZ; ISSN: 0344-5704

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have previously reported that multidrug (MDR)-reversal activity can be exerted by compds. in which two ring structures of certain types are connected by one alkyl bridge to a secondary or tertiary amine group. In the present investigation we studied the MDR-reversal activity of compds. in which the two ring structure were connected by sep. alkyl bridges to the amine group. The structure-activity relationship of these compds. verified previous findings on the structural features that support MDR-reversal activity as well as the features that reduce such activity. In addition, the present study reveals addnl. chemical groups and ring structures that support MDR-reversal activity as well as those that reduce it.

IT 90-69-7, Lobeline

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); THU (Therapeutic use);

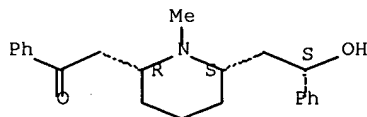
BIOL (Biological study); USES (Uses)

(multidrug resistance reversal by bis(phenylalkyl)amines and  
structurally related compds.)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-3 (Pharmacology)

IT 52-53-9, Verapamil 52-86-8, Haloperidol 54-03-5, Hexobendine  
64-96-0, U 11555A 74-31-7 78-41-1, Triparanol 90-54-0,  
Etafenone 90-69-7, Lobeline 91-75-8, Antazoline  
92-59-1, Ethylbenzylaniline 103-49-1, Dibenzylamine 140-28-3,  
N,N'-Dibenzylethylenediamine 150-59-4, Alverine 153-87-7,  
Oxypertine 357-66-4, Spirilene 366-93-8, AY 9944 469-62-5,  
Propoxyphene 475-81-0, Glaucine 493-78-7, Methaphenilene  
493-80-1, Histapyrrodine 510-74-7, Spiramide 528-52-9,  
Spasmadryl 620-40-6, Tribenzylamine 749-13-3, Trifluoperidol  
911-45-5, Clomiphene 961-71-7, Phenbenzamine 1178-99-0, U  
10520A 1480-19-9, Fluanisone 1845-11-0, Nafoxidine  
2688-77-9, Laudanosine 2784-55-6 3039-71-2, U 18666A

3625-06-7, Mebeverine 3647-71-0 3735-45-3, Vetrabutine  
 4378-36-3, Fenbutrazate 4448-96-8, Solypertine 4747-98-2,  
 Norlaudanosine 4945-47-5, Bamipine 5585-64-8, Amotriphene  
 6732-77-0, MER 37 7077-33-0, Febuverine 10448-84-7,  
 Nitromifene 10540-29-1, Tamoxifen 13002-65-8, cis-Tamoxifen  
 14728-33-7 15687-16-8, Carbiphen 15687-41-9, Oxyfedrine  
 16359-24-3, T13 16662-47-8, Gallopamil 16740-29-7, D595  
 21826-41-5, MDL 10393 21829-25-4, Nifedipine 22232-57-1,  
 Racefemine 22609-73-0, Niludipine 24360-55-2, Milipertine  
 24678-13-5, Lenperone 27076-46-6, Alpertime 30001-98-0, Ro  
 04-2250 32487-03-9, Ro 04-2359 32665-36-4, Eprozinol  
 33189-65-0, MDL 6792 34758-83-3, Zipeprol 35898-87-4, Dilazep  
 36622-29-4, (S)-Verapamil 38321-02-7, (R)-Verapamil  
 39133-31-8, Trimebutine 39562-70-4, Nitrendipine 51493-19-7  
 52618-67-4, Tioperidone 53775-12-5 54063-40-0, Fenoxedil  
 55985-32-5, Nicardipine 57010-31-8, Tiapamil 57558-44-8,  
 Secoverine 58033-02-6, D 490 58581-89-8, Azelastine  
 59170-23-9, Bevantolol 63675-72-9, Nisoldipine 64706-54-3,  
 Bepridil 65277-42-1, Ketoconazole 66085-59-4, Nimodipine  
 67018-79-5, D557 67018-81-9, D559 67018-83-1, D 525  
 67165-56-4, Diclofensine 67254-81-3, Peradoxime 67914-69-6, R  
 41300 67915-31-5, Terconazole 67915-35-9, R 42164  
 68576-86-3, Enciprazine 72509-76-3, Felodipine 72803-02-2,  
 Darodipine 75706-37-5, S 785781 77590-96-6, Flordipine  
 78370-11-3, S248 78370-13-5, Emopamil 78370-14-6, D784  
 78370-15-7, D894 83366-66-9, Nefazodone 84625-61-6,  
 Itraconazole 85247-76-3, Dagapamil 85673-87-6, Revenast  
 86656-06-6, D528 88150-42-9, Amlodipine 92302-55-1, Devapamil  
 103997-59-7, Selpazine 108704-90-1, Ro 04-2249 114697-88-0,  
 Ro 04-2360 129309-29-1 144236-78-2, S 79-0671 161161-55-3, R  
 49960 161161-56-4, Ro 04-2669 161161-57-5, SPS 1853  
 161273-29-6, Ro 04-2285

RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); **THU (Therapeutic use)**;

BIOL (Biological study); USES (Uses)

(multidrug resistance reversal by bis(phenylalkyl)amines and  
 structurally related compds.)

L51 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1976:586806 HCAPLUS Full-text

DOCUMENT NUMBER: 85:186806

TITLE: Relation between physical constants and  
 therapeutic doses of some organic bases

AUTHOR(S): Volpi, A.

CORPORATE SOURCE: Farm. "Al Moro", Mantua, Italy

SOURCE: Bollettino Chimico Farmaceutico (1976  
 ), 115(6), 466-74

CODEN: BCFAAI; ISSN: 0006-6648

DOCUMENT TYPE: Journal

LANGUAGE: Italian

AB Data are given on the molar solubility in H<sub>2</sub>O at 40° (S), an average value between the  
 mean and maximum therapeutic doses (D, in moles), and the dissociation const(s). (K<sub>1</sub>  
 and K<sub>2</sub>) of 26 mono- and 6 diacidic drugs. Correlations were sought among various  
 combinations of these parameters. An almost linear dependence was found between 1/D  
 and K/S, and a highly significant correlation between log (1/D) and log (K/S), where K  
 is K<sub>1</sub> for the monoacidic drugs and (K<sub>1</sub>K<sub>2</sub>)<sup>1/2</sup> for the diacidic drugs. No significant  
 correlations were found between log K<sub>1</sub> and log (1/D), between log K<sub>1</sub> and log S, or  
 between log (1/D) and log S.

IT 90-69-7

RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); **THU (Therapeutic use)**;

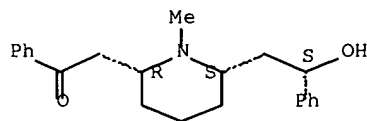
BIOL (Biological study); USES (Uses)

(pharmacol. of, phys. consts. in relation to)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-  
 piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-13 (Pharmacodynamics)

IT 50-13-5 50-36-2 50-55-5 51-05-8 51-34-3 51-43-4  
 51-55-8, biological studies 56-54-2 57-24-9 57-27-2,  
 biological studies 57-47-6 58-15-1 58-74-2 76-57-3  
 76-99-3 87-00-3 90-39-1 **90-69-7** 92-13-7 115-37-7  
 125-29-1 125-30-4 130-95-0 146-48-5 299-42-3 302-27-2  
 458-88-8 483-18-1 561-27-3 644-26-8 1435-55-8 2531-04-6  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); **THU (Therapeutic use)**;  
 BIOL (Biological study); USES (Uses)  
 (pharmacol. of, phys. consts. in relation to)

L51 ANSWER 29 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1970:41362 HCAPLUS Full-text

DOCUMENT NUMBER: 72:41362

TITLE: Bronchopulmonary and gastrointestinal effects of lobeline

AUTHOR(S): Cambar, P. J.; Shore, S. R.; Aviado, D. M.

CORPORATE SOURCE: Sch. of Med., Univ. of Pennsylvania, Philadelphia, PA, USA

SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1969), 177(1), 1-27  
 CODEN: AIPTAK; ISSN: 0003-9780

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lobeline increased pulmonary resistance in anesthetized dogs and rats, accompanied by variable effects on pulmonary compliance, aortic blood pressure, and heart rate. Intestinal motility was also inhibited in dogs, partly as a reflex elicited by inhalation of lobeline in aerosol form. The natural form of lobeline was more consistent than the synthetic form in inhibiting intestinal motility, and this inhibition was partly reduced but not completely blocked by vagotomy, indicating that a reflex mediated by the vagus is an important but not the exclusive cause of inhibition. The role of this effect in mediating the anorexia known to occur with lobeline could not be explored in the rat because the animal was suitable only for demonstration of centrally acting drugs.

IT 134-64-5

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(pharmacology of)

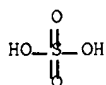
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

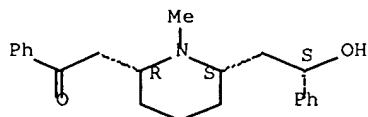


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



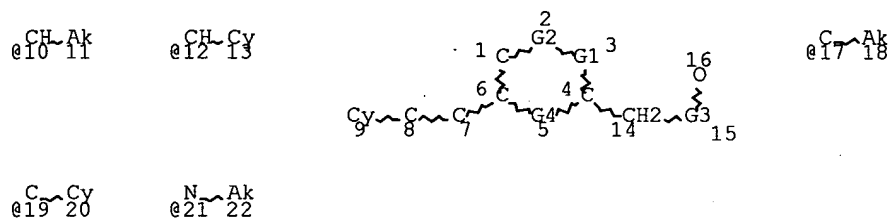
CC 15 (Pharmacodynamics)

IT 134-64-5

RL: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(pharmacology of)

=&gt; =&gt; d que stat 153

L5 STR



REP G1=(0-4) C

VAR G2=CH2/10/12

VAR G3=CH/17/19

VAR G4=NH/21

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 16

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L6 SCR 1838

L9 SCR 1100

L10 SCR 1992

L12 SCR 1918 OR 2043

L14 451 SEA FILE=REGISTRY SSS FUL L5 AND L6 AND L9 AND L10 NOT  
L12

L17 969 SEA FILE=HCAPLUS ABB=ON PLU=ON L14

L18 QUE ABB=ON PLU=ON PHARMAC?/SC, SX

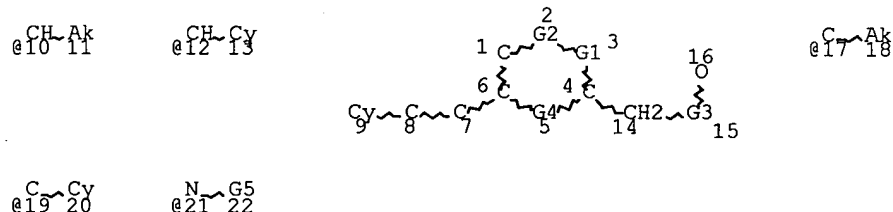
L20 703 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L18

L26 617 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND 1907-1999/PY, P  
RY

L27 QUE ABB=ON PLU=ON CNS OR CENTRAL(3A) NERVOUS(3A) (SYS  
OR SYSTEM)

10/813,647

L28 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND L27  
 L35 88 SEA FILE=HCAPLUS ABB=ON PLU=ON L14/THU  
 L36 33 SEA FILE=HCAPLUS ABB=ON PLU=ON L35 AND L26  
 L37 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L36 OR L28  
 L38 QUE ABB=ON PLU=ON (DRUG? OR NARCOT?) (2A) (ABUSE# OR A  
 BUSING OR ADDICT? OR TREAT?)  
 L39 1540 SEA FILE=HCAPLUS ABB=ON PLU=ON ANOREXIA/CT  
 L40 672 SEA FILE=HCAPLUS ABB=ON PLU=ON BULIMIA/CT  
 L41 QUE ABB=ON PLU=ON EAT?(2A) (DISORDER? OR DISEASE) OR  
 L39 OR L40  
 L42 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND L41  
 L43 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND (ANOREXIA? OR  
 BULIMIA?)  
 L44 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L37 OR L42 OR L43  
 L45 STR



REP G1=(0-4) C  
 VAR G2=CH2/10/12  
 VAR G3=CH/17/19  
 VAR G4=NH/21  
 VAR G5=ME/ET/N-PR/I-PR  
 NODE ATTRIBUTES:  
 CONNECT IS E1 RC AT 16  
 DEFAULT MLEVEL IS ATOM  
 GGCAT IS UNS AT 9  
 GGCAT IS UNS AT 13  
 GGCAT IS UNS AT 20  
 DEFAULT ECLEVEL IS LIMITED  
 ECOUNT IS M5-X6 C AT 9  
 ECOUNT IS M1-X4 C AT 11  
 ECOUNT IS M5-X6 C AT 13  
 ECOUNT IS M1-X4 C AT 18  
 ECOUNT IS M5-X6 C AT 20

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L47 171 SEA FILE=REGISTRY SUB=L14 SSS FUL L45  
 L49 82 SEA FILE=HCAPLUS ABB=ON PLU=ON L47/THU  
 L50 80 SEA FILE=HCAPLUS ABB=ON PLU=ON L49 AND (L18 OR L27  
 OR L38 OR L41)  
 L51 29 SEA FILE=HCAPLUS ABB=ON PLU=ON L50 AND 1907-1999/PY,P  
 RY  
 L53 25 SEA FILE=HCAPLUS ABB=ON PLU=ON L44 NOT L51

=> d 153 1-25 ibib abs hitstr hitind

L53 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:80353 HCAPLUS Full-text  
 DOCUMENT NUMBER: 140:128284  
 TITLE: Preparation of 2,6-distyrylpiperidines as  
 modulators of nicotinic acetylcholine receptor

mediated neurotransmitter release, uptake and storage

INVENTOR(S): Crooks, Peter A.; Dwoskin, Linda; Miller, Dennis Keith; Grinevich, Vladimir P.; Norrholm, Seth Davin; Zheng, Guangrong

PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA

SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S. 6,455,543.  
CODEN: USXXCO

DOCUMENT TYPE: Patent

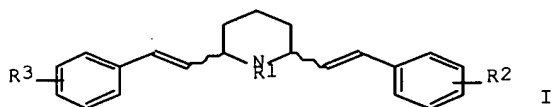
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
US 2004019081	A1	20040129	US 2002-163633	2002 0607
			<--	
US 6703406	B2	20040309		
US 6455543	B1	20020924	US 2000-628557	2000 0728
			<--	
PRIORITY APPLN. INFO.:			US 1999-146144P	P 1999 0730
			<--	
			US 2000-628557	A2 2000 0728

OTHER SOURCE(S): MARPAT 140:128284  
GI



AB Title compds. [I; R1 = H, Me, CD3, CT3, Et, alkyl cycloalkyl, vinyl, allyl, alkenyl, benzyl, phenylethyl; R2, R3 = H, Me, Et, alkyl, cycloalkyl, vinyl, allyl, alkenyl, benzyl, phenylethyl, etc.], were prepared. Thus, L-lobeline hemisulfate was stirred with NaBH4 in EtOH at 0° for 1 h to give lobelandine. The latter was stirred 24 h in 85% H3PO4 to give cis-2,6-di-trans-styrylpiperidine (II) and the trans-isomer. II inhibited nicotine-evoked [3H]-dopamine overflow at  $\alpha 3\beta 2$  receptors with IC50 = 0.03  $\mu$ M.

IT 134-64-5

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of distyrylpiperidines as modulators of nicotinic acetylcholine receptor mediated neurotransmitter release, uptake and storage)

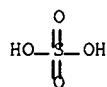
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

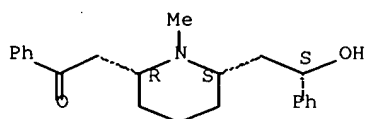


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



IT 552-72-7P, Lobelanidine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

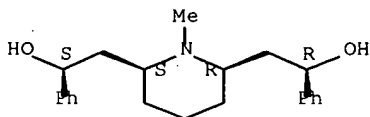
(Preparation); RACT (Reactant or reagent)

(preparation of distyrylpiperidines as modulators of nicotinic acetylcholine receptor mediated neurotransmitter release, uptake and storage)

RN 552-72-7 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-,  
( $\alpha R, \alpha' S, 2R, 6S$ )-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IC ICM A61K031-445

ICS A61K051-00

INCL 514317000; 424001110

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

ST distyrylpiperidine prepn nicotinic acetylcholine receptor mediated neurotransmitter release modulator; dopamine norepinephrine serotonin release uptake storage inhibitor distyrylpiperidine prepn; piperidine distyryl prepn **cns** disease treatment

IT Alzheimer's disease

Central nervous system, disease

Cognitive disorders

Drug dependence

Eating disorders

Motion sickness

Myasthenia gravis

Narcolepsy

Pain

Parkinson's disease

Schizophrenia

Sleep disorders

(treatment; preparation of distyrylpiperidines as modulators of  
nicotinic acetylcholine receptor mediated neurotransmitter  
release, uptake and storage)

IT 134-64-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of distyrylpiperidines as modulators of nicotinic  
acetylcholine receptor mediated neurotransmitter release,  
uptake and storage)

IT 552-72-7P, Lobelanidine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation of distyrylpiperidines as modulators of nicotinic  
acetylcholine receptor mediated neurotransmitter release,  
uptake and storage)

L53 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:432890 HCAPLUS Full-text

DOCUMENT NUMBER: 135:46204

TITLE: Preparation of 4-phenyl-2-(2-oxo-2-  
piperazinylethyl)-1,4-dihydropyridine-3,5  
dicarboxylates as bradykinin antagonists

INVENTOR(S): Okumura, Yoshiyuki; Kawamura, Mitshuriro;  
Kawai, Makoto; Murase, Noriaki; Ikeda,  
Takafumi

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1106615	A1	20010613	EP 2000-310792	2000 1205
<--				
EP 1106615	B1	20030305		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 233760	E	20030315	AT 2000-310792	2000 1205
<--				
ES 2191598	T3	20030916	ES 2000-310792	2000 1205
<--				
JP 2001192382	A2	20010717	JP 2000-373446	2000 1207
<--				
CA 2327946	AA	20010610	CA 2000-2327946	2000 1208
<--				
BR 2000005826	A	20011211	BR 2000-5826	2000 1211
<--				
US 2002042421	A1	20020411	US 2001-964907	2001



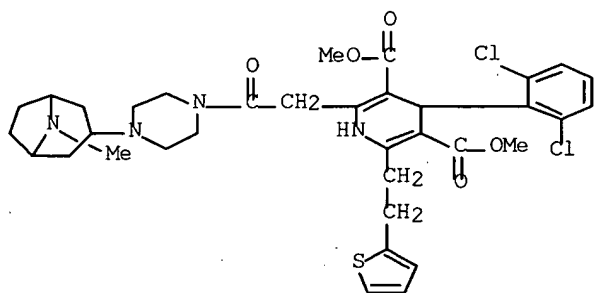
US 2003176445 A1 20030918 US 2003-366486 0927  
 2003  
 0213  
 <--  
 PRIORITY APPLN. INFO.: US 1999-170033P P 1999  
 1210  
 <--  
 US 2000-723252 A1 2000  
 1127  
 US 2001-964907 B1 2001  
 0927  
 US 2002-161026 B1 2002  
 0603  
 OTHER SOURCE(S): MARPAT 135:46204  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT  
 \*

AB Title compds. (I) [wherein A = independently halo; Y = (CH<sub>2</sub>)<sub>m</sub>, CO, or SO; R1 and R2 = independently alkyl; R3 = (un)substituted bicycloalkyl, azacycloalkyl, or azabicycloalkyl; R4 = (un)substituted thiazolyl, imidazolyl, or oxazolyl; R5 = H or alkyl; m = 0-2; n = 0-5; or the pharmaceutically acceptable salts thereof] were prepared as bradykinin antagonists for the treatment of inflammation, allergic rhinitis, pain, etc. For example, II was formed in a multi-step sequence involving the reaction of Me 3-(2,6-dichlorophenyl)-2-[3-(1,3-thiazol-2-yl)propanoyl]-2- propenoate with di-Me 3-amino-2-pentenedioate to give the 2-[1,4-dihydro-3,5-bis(methoxycarbonyl)-2-pyridinyl]acetic acid (85%), followed by amidation with 4-(3-methylbicyclo[3.2.1]oct-3-yl)piperazine (73%). In recombinant human bradykinin B2 receptor expressing CHO-K1 cells, I inhibited the binding of bradykinin to its receptor sites with IC<sub>50</sub> values of 1 nM to 30 nM.

IT 344436-19-7  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (comparison compound; preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-dihydropyridine-3,5-dicarboxylates for treatment of inflammation, asthma, allergic rhinitis, pain, and other bradykinin related disorders)

RN 344436-19-7 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thienyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



IT 344434-28-2P 344434-38-4P

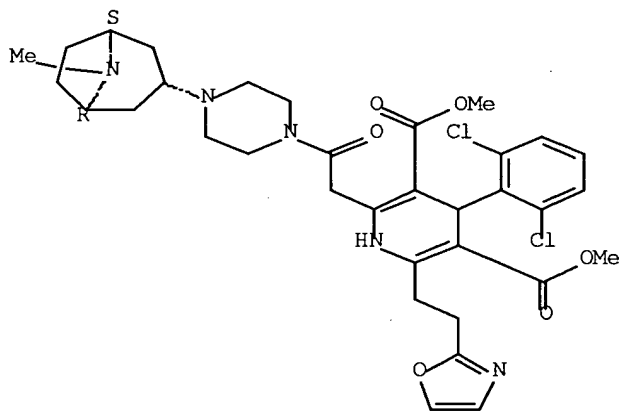
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-dihydropyridine-3,5-dicarboxylate bradykinin antagonists by reaction of benzylidenes with enamines and addition of piperazines)

RN 344434-28-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-oxazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 344434-38-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3S)-1-azabicyclo[2.2.2]oct-3-yl-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

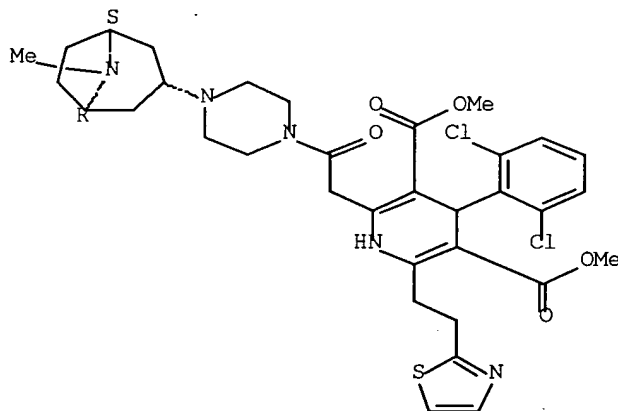
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of 4-phenyl-2-(2-oxo-2-piperazinyloethyl)-1,4-dihydropyridine-3,5-dicarboxylate bradykinin antagonists by reaction of benzylidenes with enamines and addition of piperazines)

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-  
piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl  
ester, (4R)-rel-(-)- (9CI) (CA INDEX NAME)

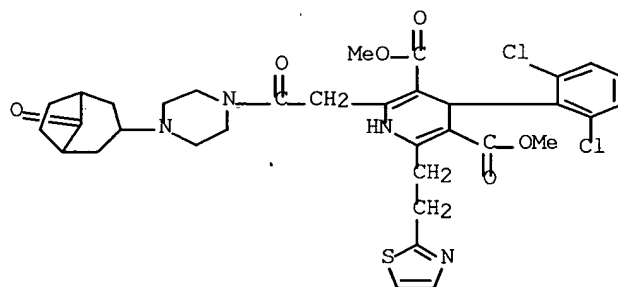
Page 80

RN 344434-19-1 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-  
 piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester  
 (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 344435-96-7 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-oxo-2-[4-(8-oxobicyclo[3.2.1]oct-3-yl)-1-piperazinyl]ethyl]-6-  
 [2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



IT 344433-95-0P 344433-97-2P 344433-99-4P  
 344434-01-1P 344434-03-3P 344434-05-5P  
 344434-07-7P 344434-09-9P 344434-11-3P  
 344434-13-5P 344434-15-7P 344434-17-9P  
 344434-24-8P 344434-26-0P 344434-30-6P  
 344434-32-8P 344434-34-0P 344434-36-2P  
 344434-40-8P 344434-42-0P 344434-44-2P  
 344434-46-4P 344434-48-6P 344434-50-0P  
 344434-52-2P 344434-54-4P 344434-56-6P  
 344434-58-8P 344434-60-2P 344434-62-4P  
 344434-64-6P 344434-67-9P 344434-69-1P  
 344434-71-5P 344434-73-7P 344434-75-9P  
 344434-77-1P 344434-79-3P 344434-81-7P  
 344434-83-9P 344434-85-1P 344434-87-3P  
 344434-89-5P 344436-14-2P 344436-15-3P  
 344436-16-4P 344436-17-5P 344436-18-6P  
 344570-44-1P 344570-45-2P

RL: BAC (Biological activity or effector, except adverse); BSU

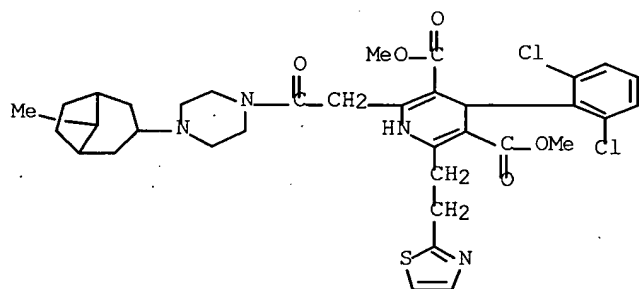
10/813,647

(Biological study, unclassified); SPN (Synthetic preparation);  
**THU (Therapeutic use)**; BIOL (Biological study); PREP  
 (Preparation); USES (Uses)

(preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-  
 dihydropyridine-3,5-dicarboxylate bradykinin antagonists by  
 reaction of benzylidenes with enamines and addition of  
 piperazines)

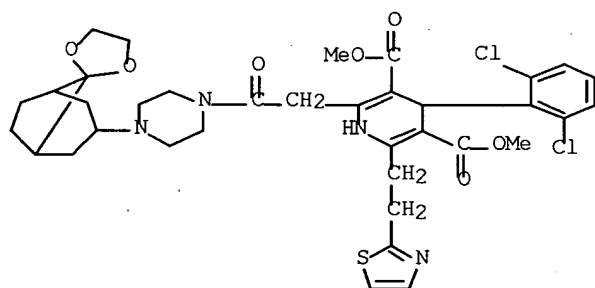
RN 344433-95-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-[4-(8-methylbicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-  
 oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA  
 INDEX NAME)



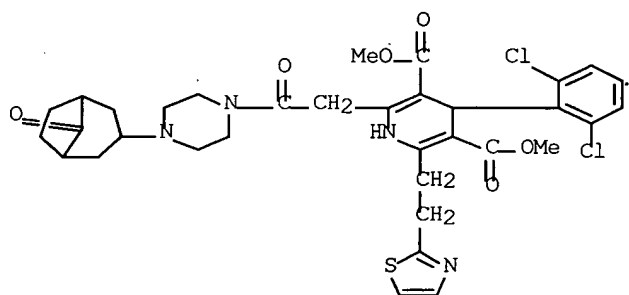
RN 344433-97-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-oxo-2-(4-spiro[bicyclo[3.2.1]octane-8,2'-[1,3]dioxolan]-3-yl-  
 1-piperazinyl)ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester  
 (9CI) (CA INDEX NAME)



RN 344433-99-4 HCAPLUS

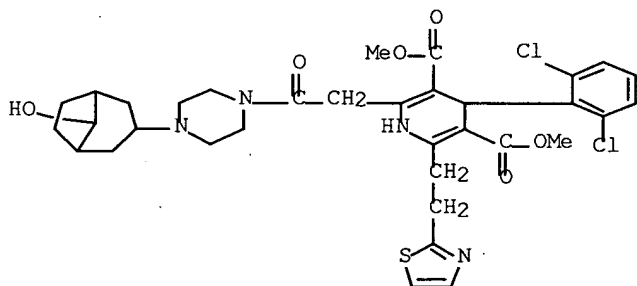
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-oxo-2-[4-(8-oxobicyclo[3.2.1]oct-3-yl)-1-piperazinyl]ethyl]-6-  
 [2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI)  
 (CA INDEX NAME)



● HCl

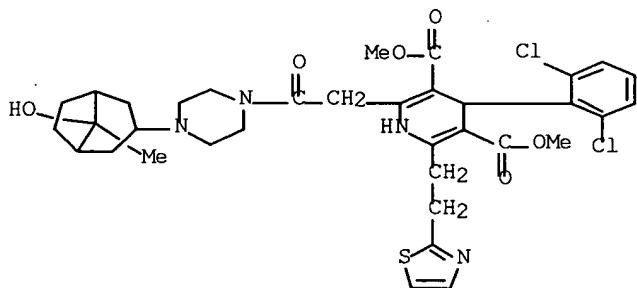
RN 344434-01-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-hydroxybicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344434-03-3 HCAPLUS

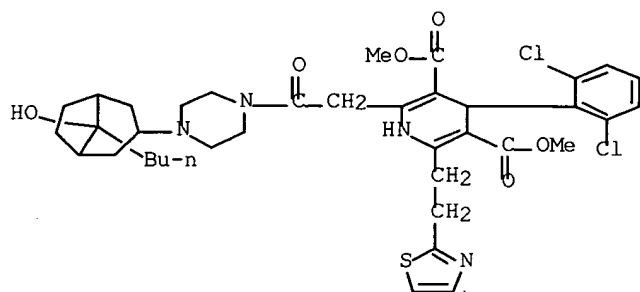
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-hydroxy-8-methylbicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344434-05-5 HCAPLUS

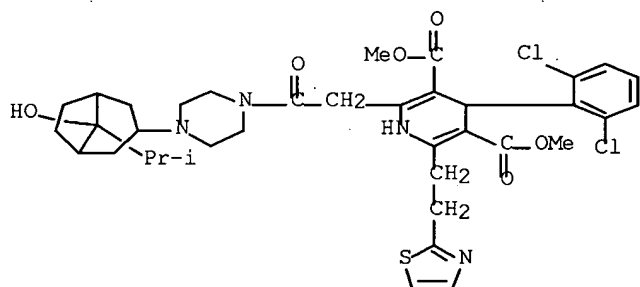
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(8-butyl-8-hydroxybicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester

ester (9CI) (CA INDEX NAME)



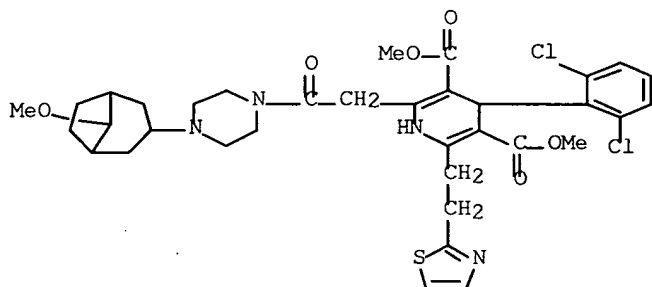
RN 344434-07-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[8-hydroxy-8-(1-methylethyl)bicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



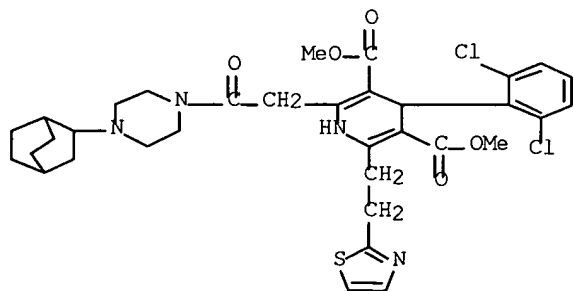
RN 344434-09-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methoxybicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



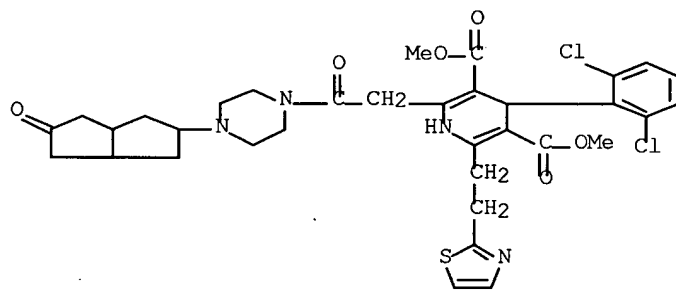
RN 344434-11-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-(4-bicyclo[2.2.2]oct-2-yl-1-piperazinyl)-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



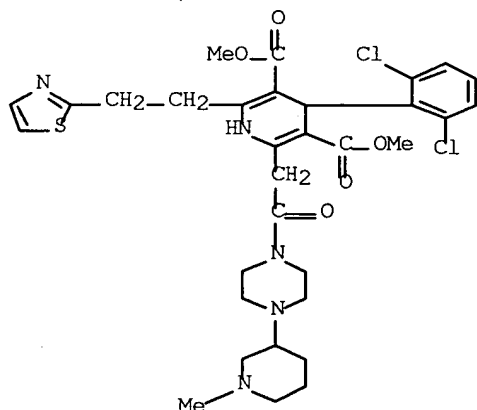
RN 344434-13-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(octahydro-5-oxo-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344434-15-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(1-methyl-3-piperidiny)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



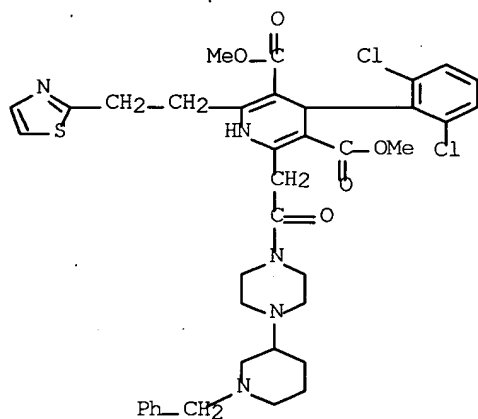
RN 344434-17-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[1-(phenylmethyl)-3-piperidiny]-1-piperazinyl]-1-ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



10/813,647

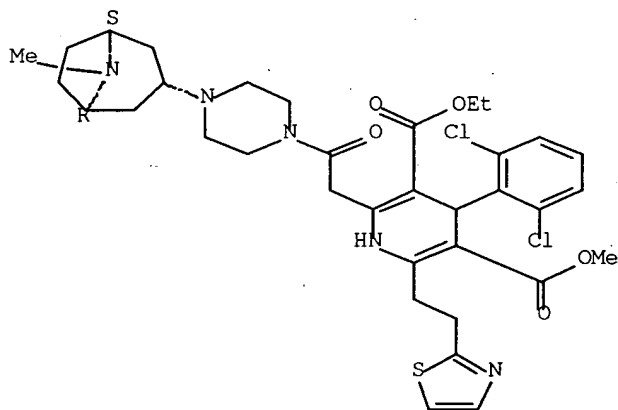
piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI)  
(CA INDEX NAME)



RN 344434-24-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, 3-ethyl 5-methyl ester (9CI) (CA INDEX NAME)

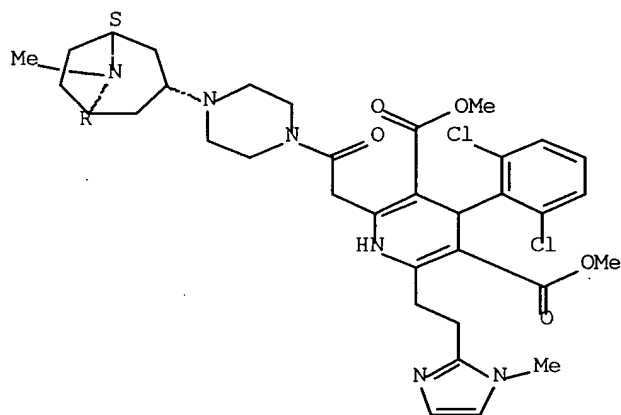
Relative stereochemistry.



RN 344434-26-0 HCAPLUS

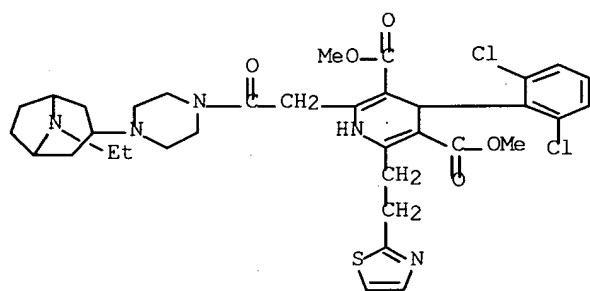
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(1-methyl-1H-imidazol-2-yl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



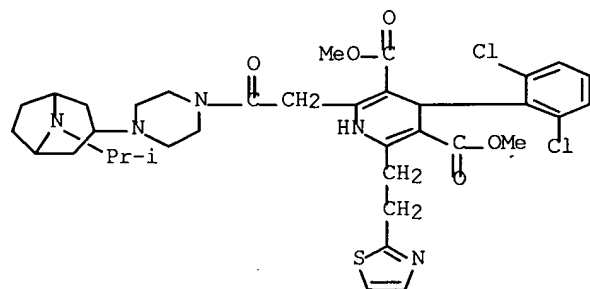
RN 344434-30-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(8-ethyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344434-32-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[8-(1-methylethyl)-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

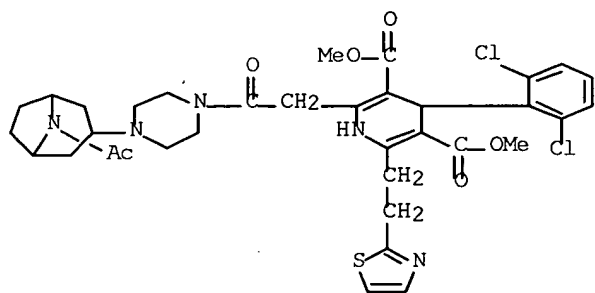


RN 344434-34-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(8-acetyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-

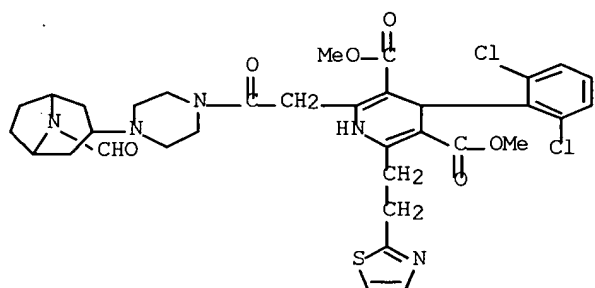
10/813,647

dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344434-36-2 HCAPLUS

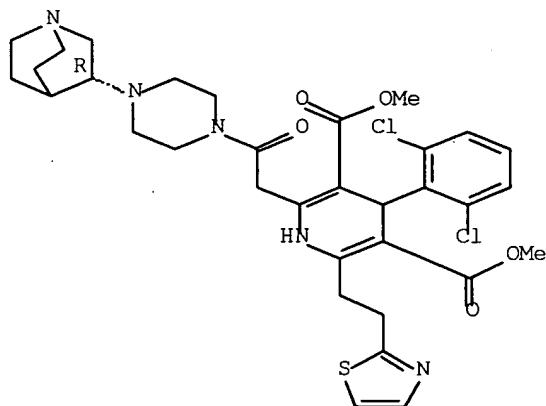
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(8-formyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344434-40-8 HCAPLUS

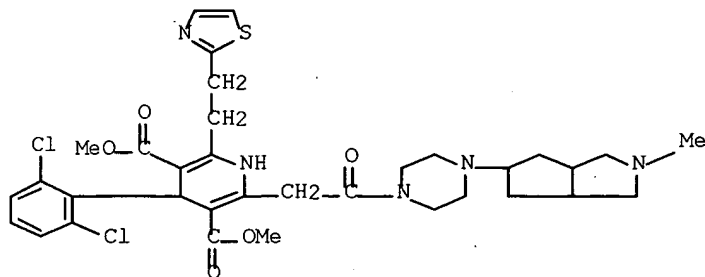
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



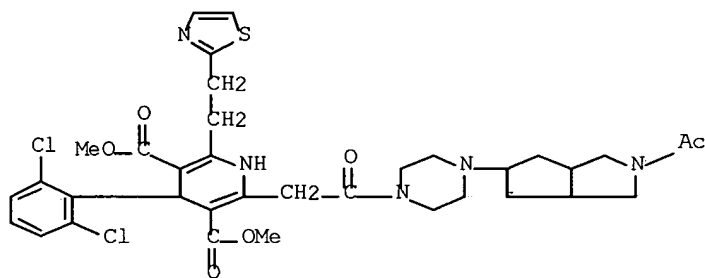
RN 344434-42-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(octahydro-2-methylcyclopenta[c]pyrrol-5-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



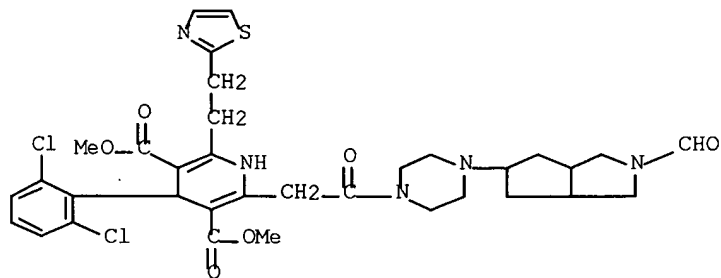
RN 344434-44-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(2-acetyloctahydrocyclopenta[c]pyrrol-5-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



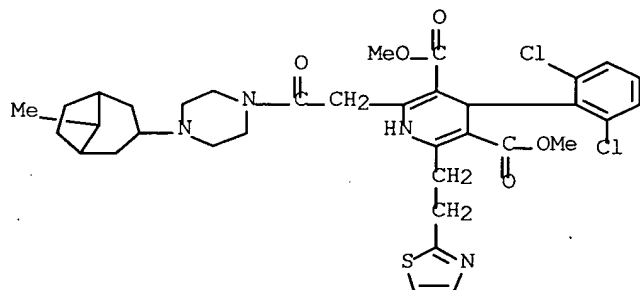
RN 344434-46-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(2-formyloctahydrocyclopenta[c]pyrrol-5-yl)-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344434-48-6 HCAPLUS

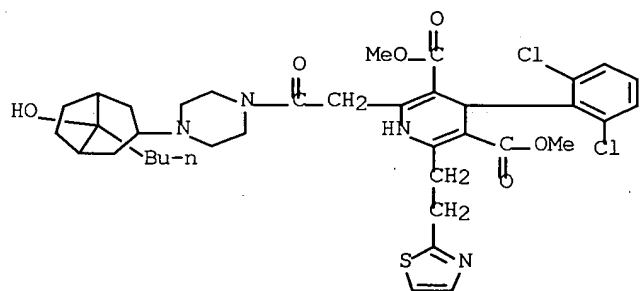
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methylbicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-50-0 HCAPLUS

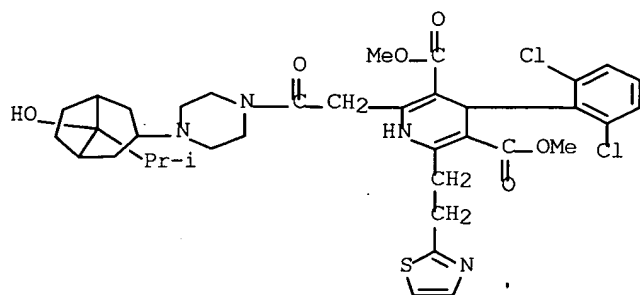
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(8-butyl-8-hydroxybicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-52-2 HCAPLUS

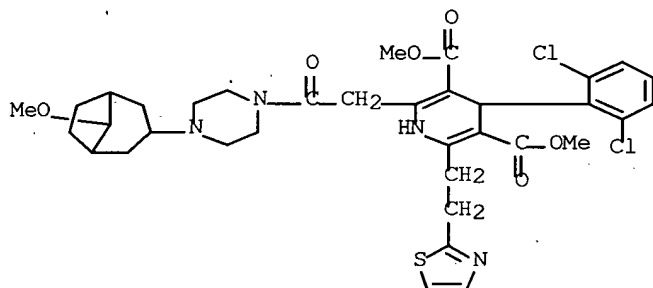
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[8-hydroxy-8-(1-methylethyl)bicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-54-4 HCAPLUS

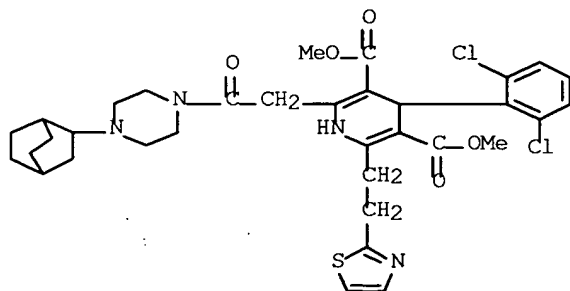
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methoxybicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-56-6 HCAPLUS

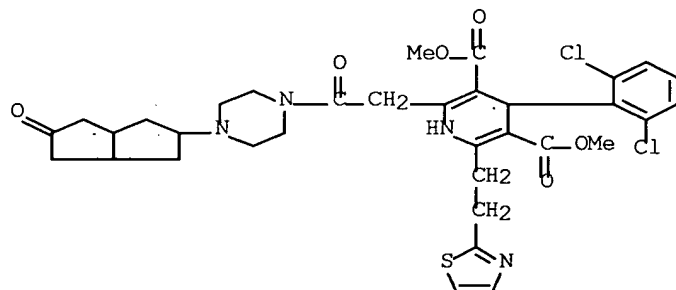
CN 3,5-Pyridinedicarboxylic acid, 2-[2-(4-bicyclo[2.2.2]oct-2-yl-1-piperazinyl)-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-58-8 HCAPLUS

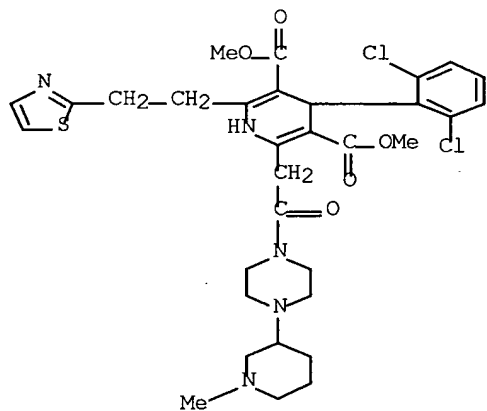
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(octahydro-5-oxo-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-60-2 HCAPLUS

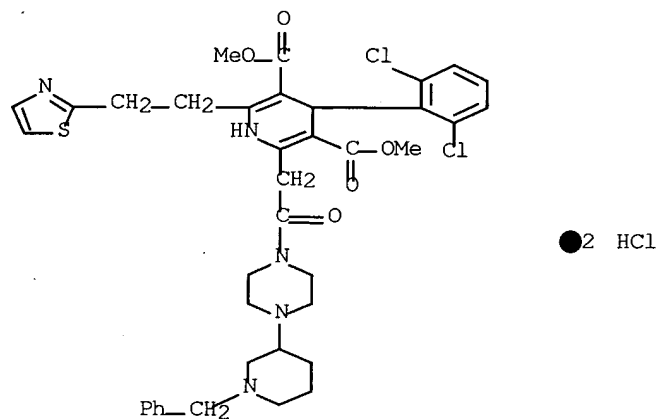
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(1-methyl-3-piperidiny)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 344434-62-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[1-(phenylmethyl)-3-piperidiny]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

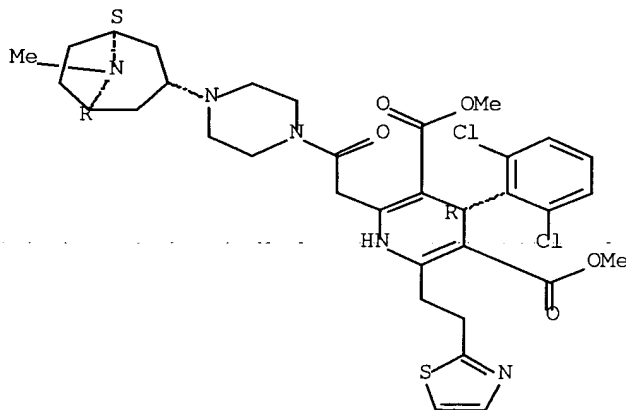


RN 344434-64-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride, (4R)-rel-(-)-(9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.

PAGE 1-A



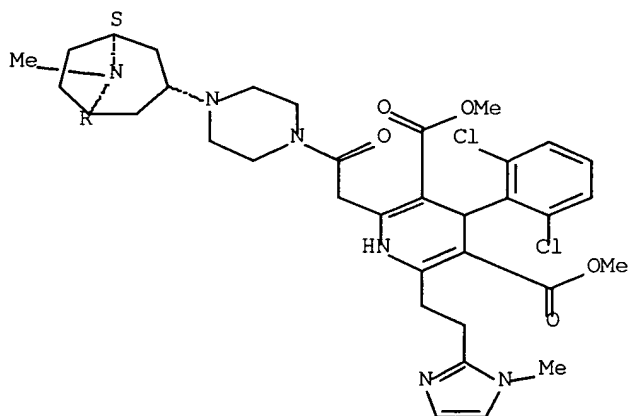
PAGE 2-A

RN 344434-67-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(1-methyl-1H-imidazol-2-yl)ethyl]-, dimethyl ester, trihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

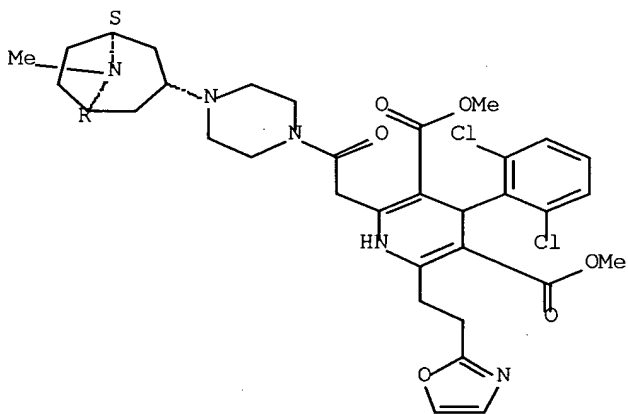




●3 HCl

RN 344434-69-1 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-  
 piperazinyl]-2-oxoethyl]-6-[2-(2-oxazolyl)ethyl]-, dimethyl ester,  
 dihydrochloride (9CI) (CA INDEX NAME)

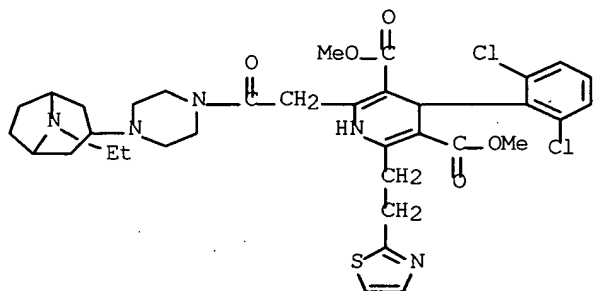
Relative stereochemistry.



●2 HCl

RN 344434-71-5 HCAPLUS

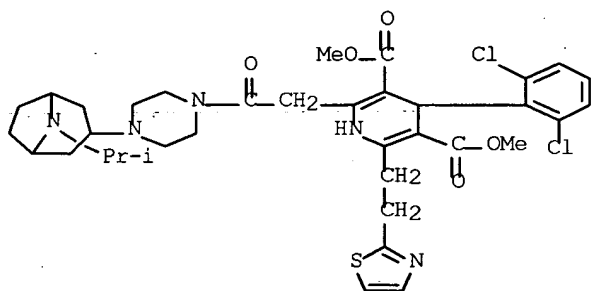
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(8-ethyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 344434-73-7 HCAPLUS

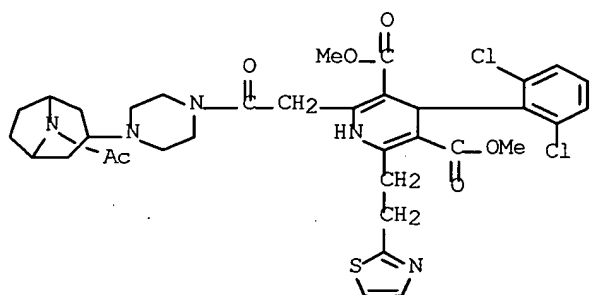
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[8-(1-methylethyl)-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 344434-75-9 HCAPLUS

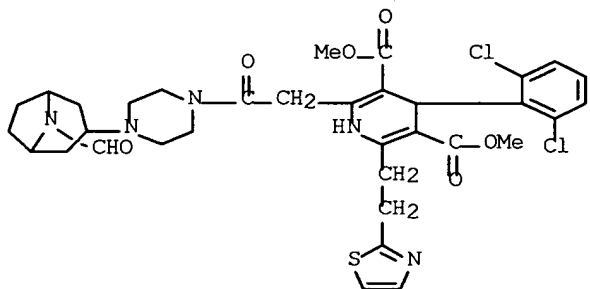
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(8-acetyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-77-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(8-formyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME).

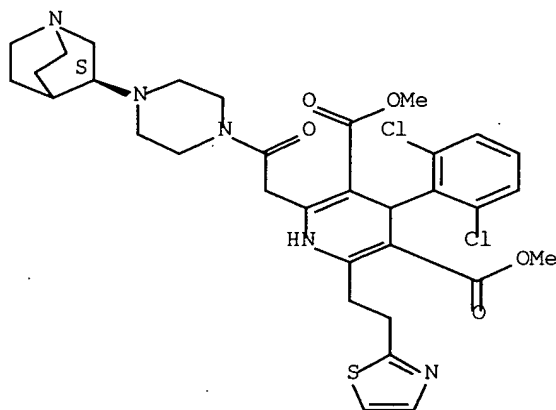


● HCl

RN 344434-79-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3S)-1-azabicyclo[2.2.2]oct-3-yl-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

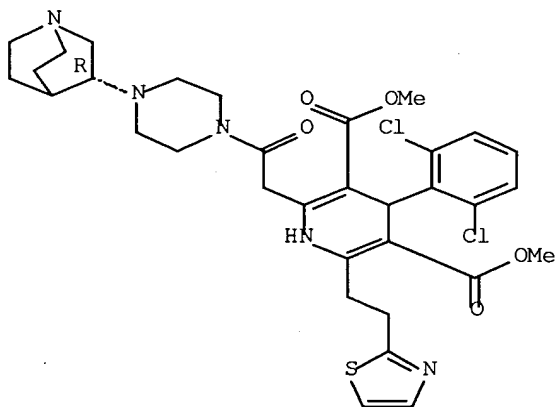
Absolute stereochemistry.



●2 HCl

RN 344434-81-7 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3R)-1-azabicyclo[2.2.2]oct-3-yl-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI)  
 (CA INDEX NAME)

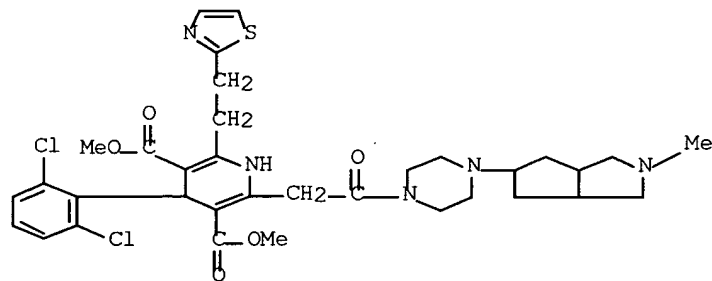
Absolute stereochemistry.



●2 HCl

RN 344434-83-9 HCAPLUS

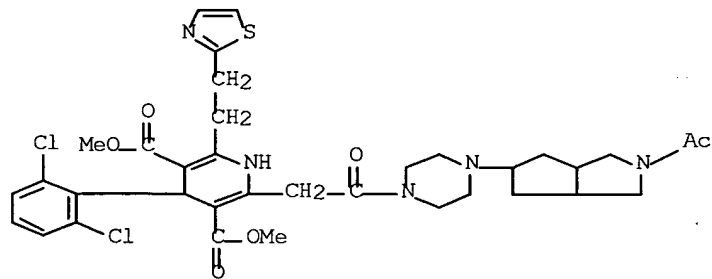
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(octahydro-2-methylcyclopenta[c]pyrrol-5-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 344434-85-1 HCAPLUS

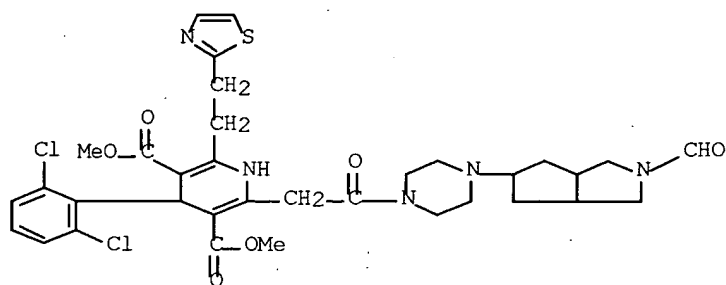
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(2-acetyloctahydrocyclopenta[c]pyrrol-5-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 344434-87-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(2-formyloctahydrocyclopenta[c]pyrrol-5-yl)-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



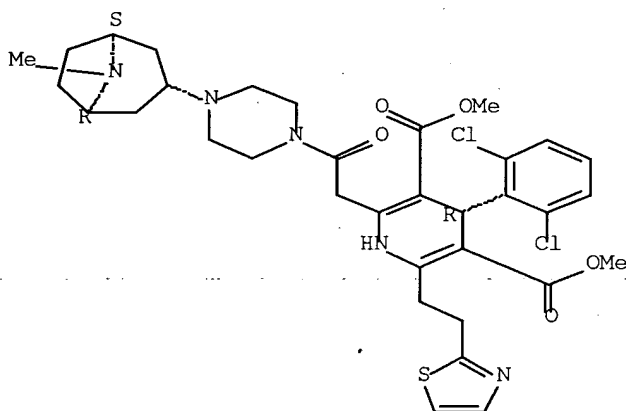
● HCl

RN 344434-89-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-[4-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-  
 piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl  
 ester, monohydrochloride, (4R)-rel-(-)- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.

PAGE 1-A

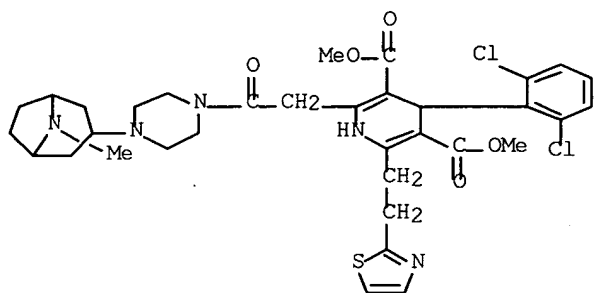


PAGE 2-A

● HCl

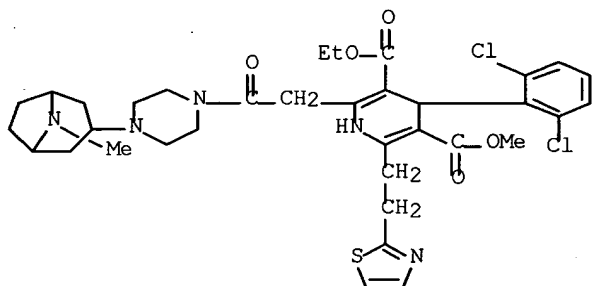
RN 344436-14-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-  
 oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA  
 INDEX NAME)



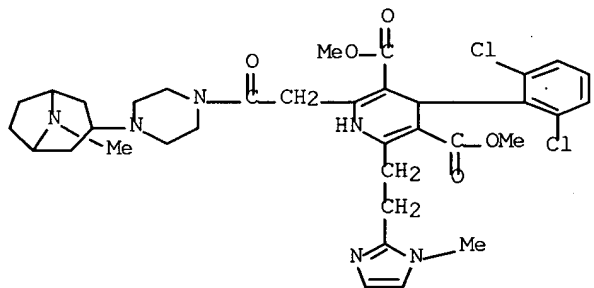
RN 344436-15-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, 3-ethyl 5-methyl ester (9CI) (CA INDEX NAME)



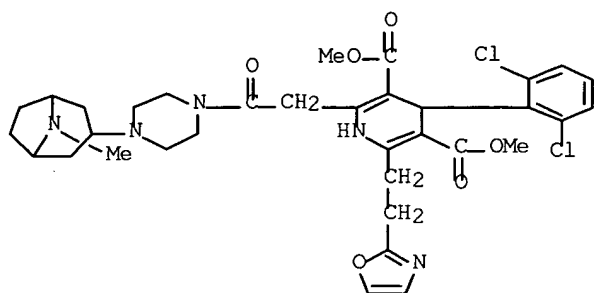
RN 344436-16-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(1-methyl-1H-imidazol-2-yl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



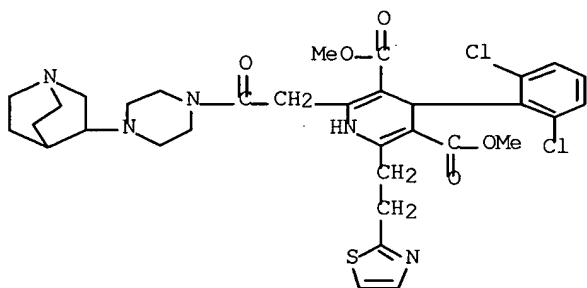
RN 344436-17-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-oxazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344436-18-6 HCAPLUS

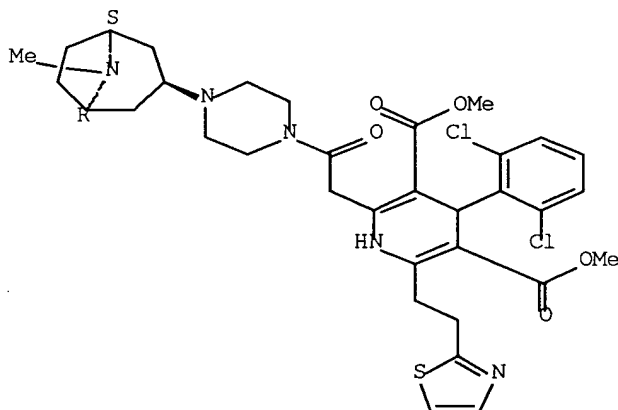
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(1-azabicyclo[2.2.2]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344570-44-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 344570-45-2 HCAPLUS

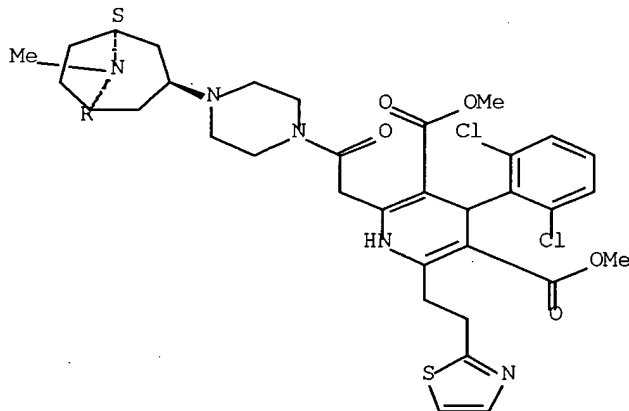
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



PAGE 2-A

●2 HCl

IC ICM C07D417-14

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

IT 344436-19-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)  
(comparison compound; preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-dihydropyridine-3,5-dicarboxylates for treatment of inflammation, asthma, allergic rhinitis, pain, and other bradykinin related disorders)

IT 344434-28-2P 344434-38-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-dihydropyridine-3,5-dicarboxylate bradykinin antagonists by reaction of benzylidenes with enamines and addition of piperazines)

IT 344434-21-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-dihydropyridine-3,5-dicarboxylate bradykinin antagonists by reaction of benzylidenes with enamines and addition of piperazines)

IT 344434-19-1P 344435-96-7P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-dihydropyridine-3,5-dicarboxylate bradykinin antagonists by reaction of benzylidenes with enamines and addition of piperazines)

IT 344433-95-0P 344433-97-2P 344433-99-4P  
 344434-01-1P 344434-03-3P 344434-05-5P  
 344434-07-7P 344434-09-9P 344434-11-3P  
 344434-13-5P 344434-15-7P 344434-17-9P  
 344434-24-8P 344434-26-0P 344434-30-6P  
 344434-32-8P 344434-34-0P 344434-36-2P  
 344434-40-8P 344434-42-0P 344434-44-2P  
 344434-46-4P 344434-48-6P 344434-50-0P  
 344434-52-2P 344434-54-4P 344434-56-6P  
 344434-58-8P 344434-60-2P 344434-62-4P  
 344434-64-6P 344434-67-9P 344434-69-1P  
 344434-71-5P 344434-73-7P 344434-75-9P  
 344434-77-1P 344434-79-3P 344434-81-7P  
 344434-83-9P 344434-85-1P 344434-87-3P  
 344434-89-5P 344436-14-2P 344436-15-3P  
 344436-16-4P 344436-17-5P 344436-18-6P  
 344570-44-1P 344570-45-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-phenyl-2-(2-oxo-2-piperazinylethyl)-1,4-dihydropyridine-3,5-dicarboxylate bradykinin antagonists by reaction of benzylidenes with enamines and addition of piperazines)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L53 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:432889 HCAPLUS Full-text

DOCUMENT NUMBER: 135:46173

TITLE: Preparation of 4-phenyl-2-thiazolylalkyl-1,4-dihydropyridine-3,5-dicarboxylates and analogs as bradykinin antagonists

INVENTOR(S): Kawai, Makoto; Murase, Noriaki; Ikeda, Takafumi; Shishido, Yuji; Nukui, Seiji; Okumura, Yoshiyuki; Kawamura, Mitsuhiro

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 60 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1106614	A1	20010613	EP 2000-310793	2000 1205
EP 1106614	B1	20040107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 257479	E	20040115	AT 2000-310793	2000 1205

PT 1106614	T	20040430	PT 2000-310793	<--	2000 1205
ES 2211460	T3	20040716	ES 2000-310793	<--	2000 1205
JP 2001187793	A2	20010710	JP 2000-373447	<--	2000 1207
JP 3651885	B2	20050525		<--	
US 2001046993	A1	20011129	US 2000-731995		2000 1207
US 6444677	B2	20020903		<--	
CA 2327925	AA	20010610	CA 2000-2327925		2000 1208
BR 2000006371	A	20010724	BR 2000-6371	<--	2000 1211
JP 2005120107	A2	20050512	JP 2004-364980	<--	2004 1216
PRIORITY APPLN. INFO.:			US 1999-170142P	P	1999 1210
			JP 2000-373447	A3	2000 1207
OTHER SOURCE(S):	MARPAT 135:46173				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT  
\*

AB Title compds. (I) [wherein A = independently halo; Y1 = (CH<sub>2</sub>)<sub>m</sub>, CO, or SO; Y2 = N or CH; R1 and R2 = independently alkyl; R3 = (un)substituted (CH<sub>2</sub>)<sub>p</sub>cycloalkyl, or (bicyclo)alkyl; R4 = (un)substituted thiazolyl, imidazolyl, or oxazolyl; X = S, NH, alkylimino, or O; R5 = H or alkyl; R6 = alkyl or halo; m = 0-2; n = 0-5; p = 0-6; or the pharmaceutically acceptable salts thereof] were prepared as bradykinin antagonists for the treatment of inflammation, asthma, allergic rhinitis, pain, etc. For example, II was synthesized in a multi-step sequence involving the reaction of Me 3-(2,6-dichlorophenyl)-2-[3-(1,3-thiazol-2-yl)propanoyl]-2-propenoate with di-Me 3-amino-2-pentenedioate to give the 2-(2-methoxy-2-oxoethyl)-1,5-dihydropyridine-3,5-dicarboxylate (85%), which was converted to the 3,5-bis(methoxycarbonyl)-1,4-dihydro-2-pyridinylacetic acid derivative (80%) and amidated with 1-(1-piperazinylmethyl)cyclohexanecarbonitrile. In recombinant human bradykinin B2 receptor expressing CHO-K1 cells, I inhibited the binding of bradykinin to its receptor sites with IC<sub>50</sub> values of 1 nM to 50 nM.

IT 344615-99-2P 344616-00-8P 344616-01-9P  
344616-02-0P 344616-03-1P 344616-04-2P  
344616-05-3P 344616-06-4P 344616-07-5P  
344616-08-6P 344616-09-7P 344616-10-0P  
344616-11-1P 344616-12-2P 344616-13-3P

344616-15-5P 344616-16-6P 344616-17-7P  
 344616-19-9P 344616-20-2P 344616-21-3P  
 344616-22-4P 344616-23-5P 344616-24-6P  
 344616-25-7P 344616-26-8P 344616-27-9P  
 344616-28-0P 344616-29-1P 344616-30-4P  
 344616-31-5P 344616-32-6P 344616-33-7P  
 344616-34-8P 344616-35-9P 344616-36-0P  
 344616-37-1P 344616-38-2P 344616-39-3P  
 344616-40-6P 344616-41-7P 344616-42-8P  
 344616-43-9P 344616-44-0P 344616-45-1P  
 344616-46-2P 344616-47-3P 344616-48-4P  
 344616-49-5P 344616-52-0P 344617-71-6P  
 344617-72-7P 344617-74-9P 344617-75-0P  
 344617-76-1P 344617-77-2P 344617-78-3P  
 344617-79-4P 344617-80-7P 344617-81-8P  
 344617-82-9P 344617-83-0P 344617-84-1P  
 344617-85-2P 344617-86-3P 344617-87-4P  
 344617-88-5P 344617-89-6P 344617-90-9P  
 344617-91-0P 344617-92-1P 344617-93-2P  
 344617-94-3P 344617-95-4P 344617-96-5P  
 344617-97-6P 344617-98-7P 344617-99-8P  
 344618-00-4P 344618-01-5P 344618-02-6P  
 344618-03-7P 344618-04-8P 344618-05-9P  
 344618-06-0P 344618-07-1P 344618-08-2P  
 344618-09-3P 344618-10-6P 344618-11-7P

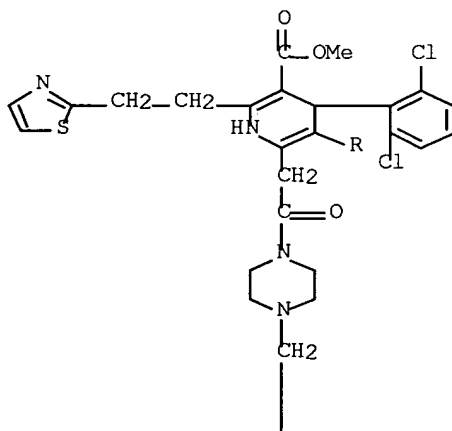
RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); SPN (Synthetic preparation);  
 THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)

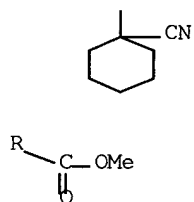
(preparation of 4-phenyl-2-thiazolylalkyl-1,4-dihydropyridine-3,5-  
 dicarboxylates and analogs by reaction of benzylidenes with  
 enamines as bradykinin antagonists)

RN 344615-99-2 HCAPLUS

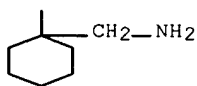
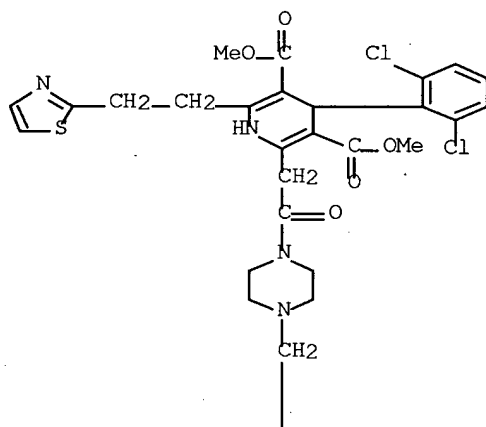
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[(1-cyanocyclohexyl)methyl]-  
 1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-  
 (2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

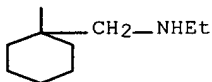
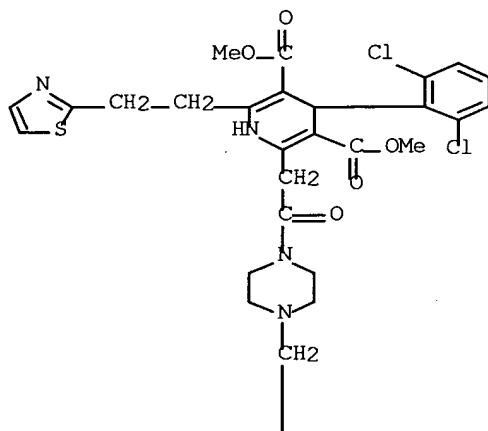




RN 344616-00-8 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-(aminomethyl)cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

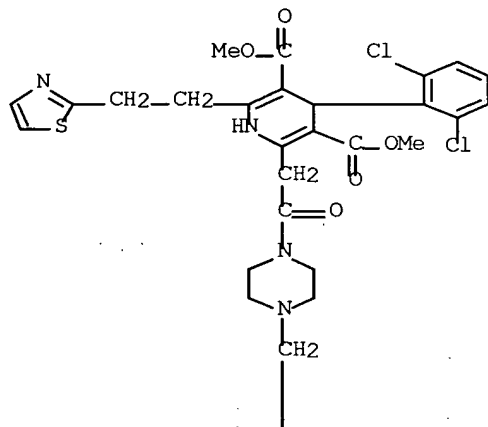


RN 344616-01-9 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-[(ethylamino)methyl]cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



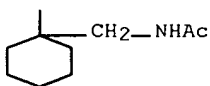
RN 344616-02-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-[(acetylamino)methyl]cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



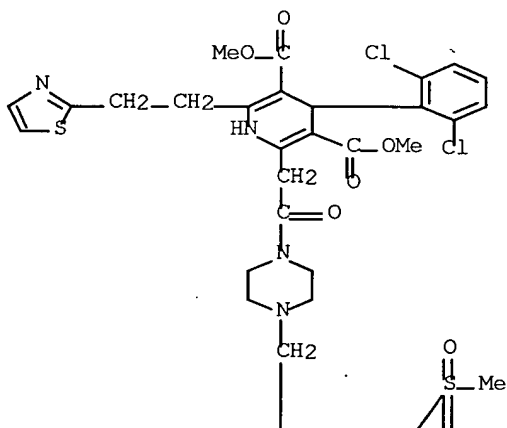
10/813,647

PAGE 2-A

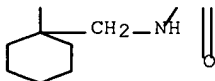


RN 344616-03-1 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[[1-[(methylsulfonyl)amino]methyl]cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

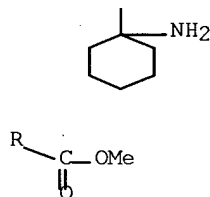
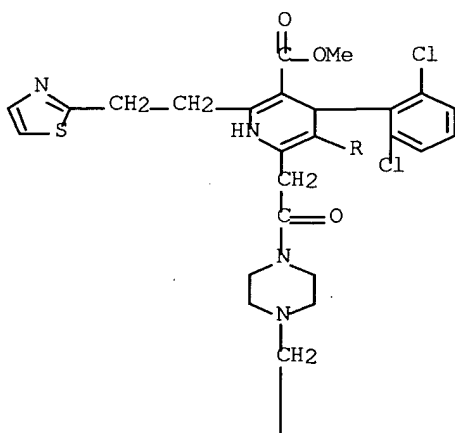
PAGE 1-A



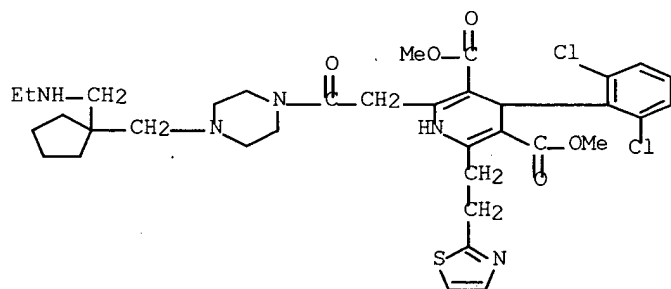
PAGE 2-A



RN 344616-04-2 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[(1-aminocyclohexyl)methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

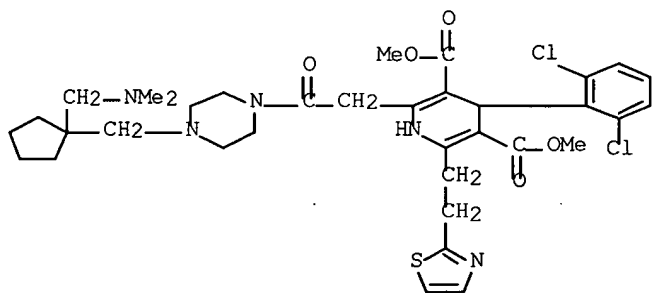


RN 344616-05-3 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-[(ethylamino)methyl]cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



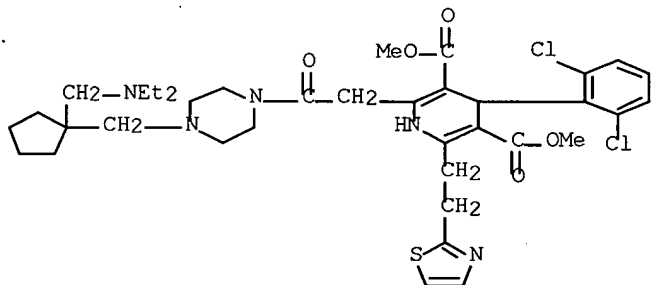
RN 344616-06-4 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-[(dimethylamino)methyl]cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)





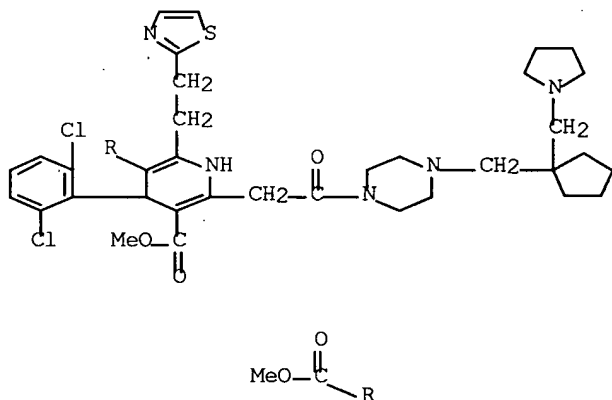
RN 344616-07-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-((diethylamino)methyl)cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344616-08-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[[1-(1-pyrrolidinylmethyl)cyclopentyl]methyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

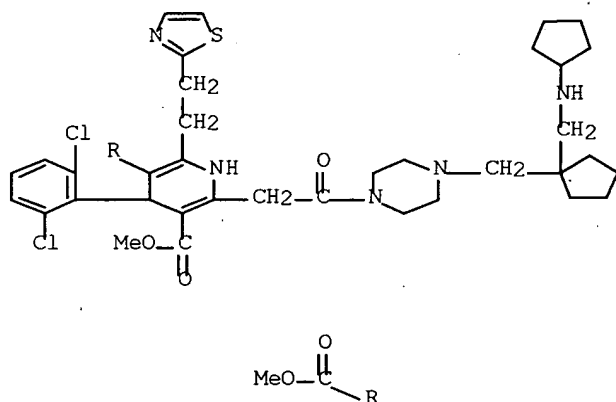


RN 344616-09-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-(cyclopentylamino)methyl]cyclopentyl]methyl]-1-piperazinyl]-2-

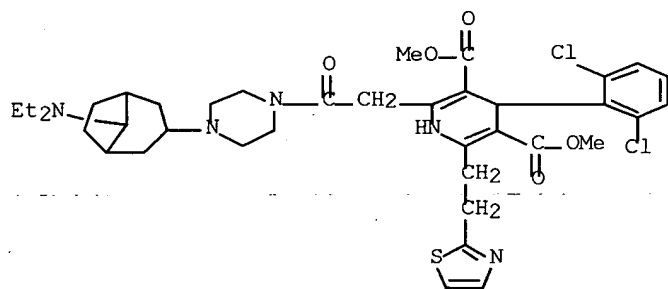
10/813,647

oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



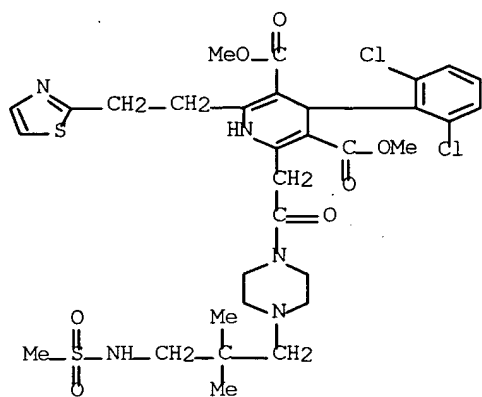
RN 344616-10-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[8-(diethylamino)bicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



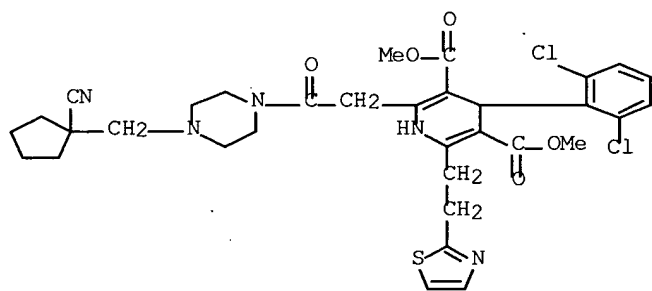
RN 344616-11-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[2,2-dimethyl-3-[(methylsulfonyl)amino]propyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



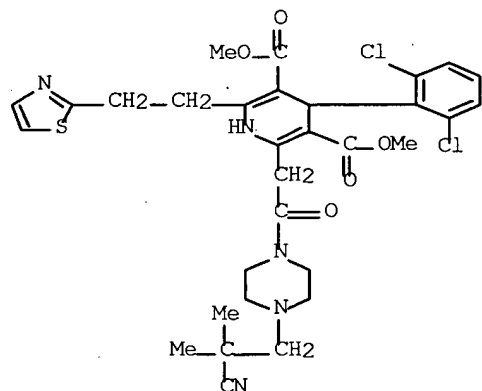
RN 344616-12-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[(1-cyanocyclopentyl)methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



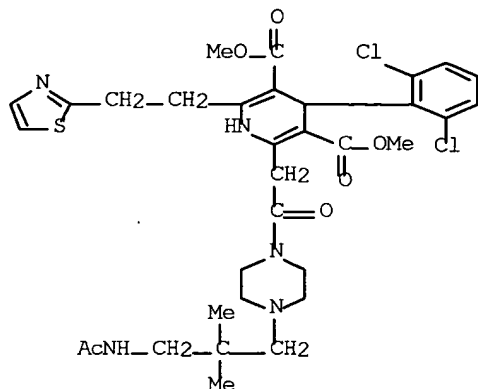
RN 344616-13-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(2-cyano-2-methylpropyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



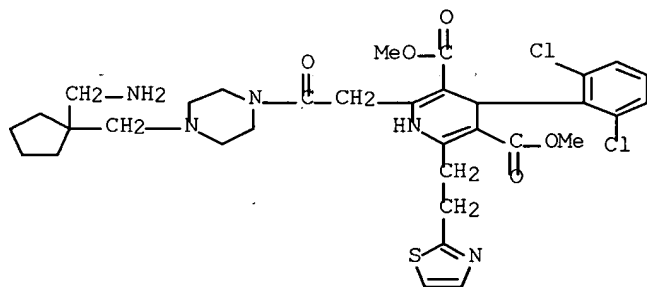
RN 344616-15-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[3-(acetylamino)-2,2-dimethylpropyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



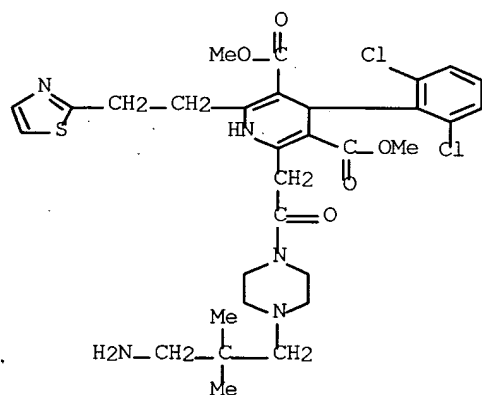
RN 344616-16-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-(aminomethyl)cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



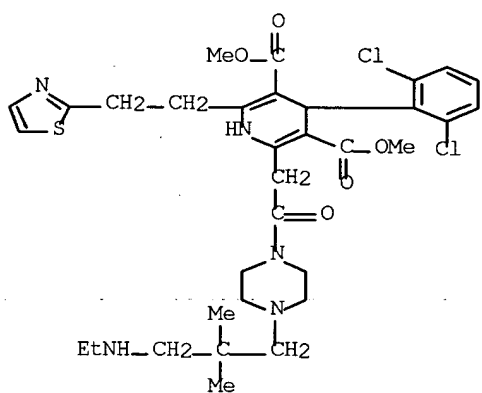
RN 344616-17-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3-amino-2,2-dimethylpropyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



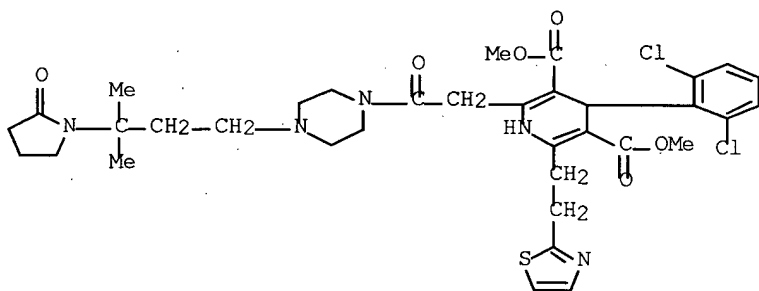
RN 344616-19-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-(ethylamino)-2,2-dimethylpropyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



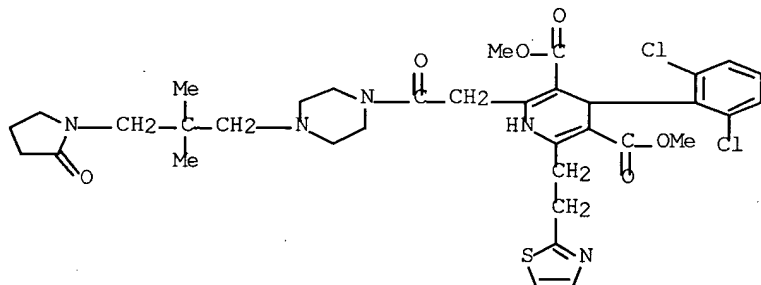
RN 344616-20-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[3-methyl-3-(2-oxo-1-pyrrolidinyl)butyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



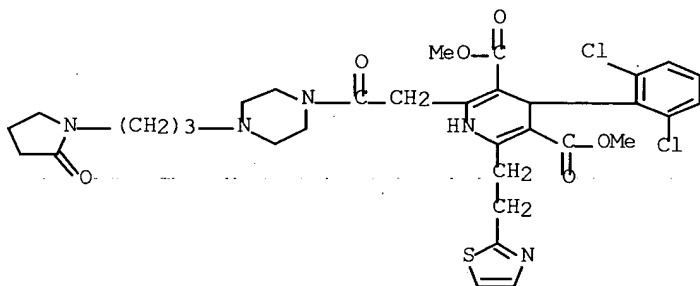
RN 344616-21-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[2,2-dimethyl-3-(2-oxo-1-pyrrolidinyl)propyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



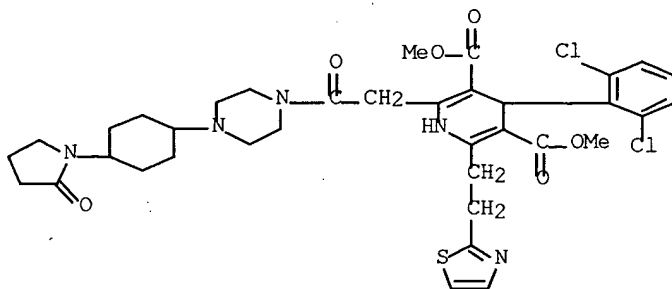
RN 344616-22-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[3-(2-oxo-1-pyrrolidinyl)propyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



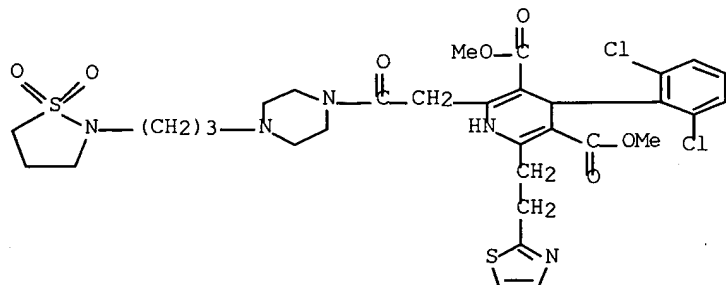
RN 344616-23-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[4-(2-oxo-1-pyrrolidinyl)cyclohexyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



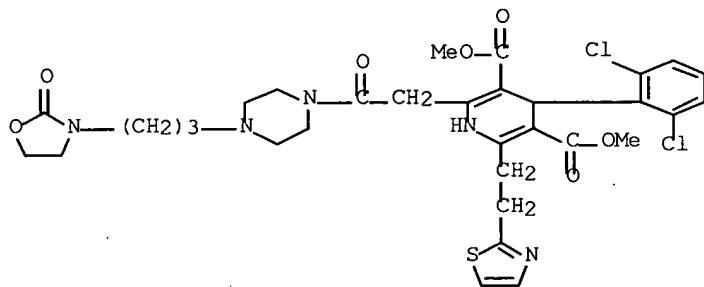
RN 344616-24-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-(1,1-dioxido-2-isothiazolidinyl)propyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



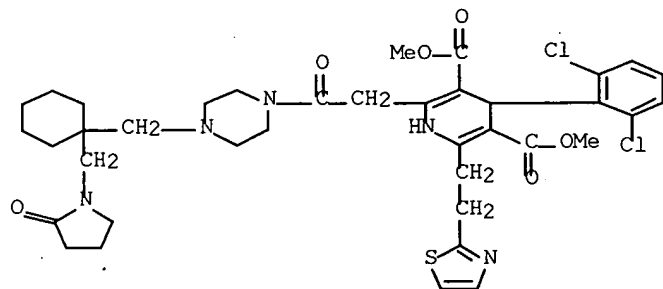
RN 344616-25-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[3-(2-oxo-3-oxazolidinyl)propyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



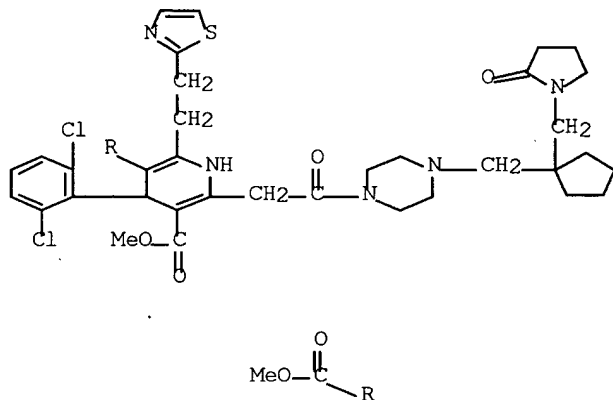
RN 344616-26-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[1-[(2-oxo-1-pyrrolidinyl)methyl]cyclohexyl]methyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



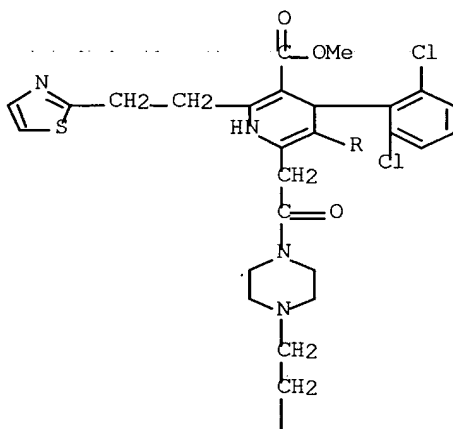
RN 344616-27-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-oxo-2-[4-[[1-[(2-oxo-1-pyrrolidinyl)methyl]cyclopentyl]methyl  
 ]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester  
 (9CI) (CA INDEX NAME)



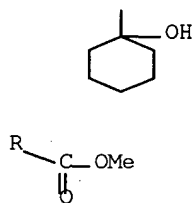
RN 344616-28-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-[4-[2-(1-hydroxycyclohexyl)ethyl]-1-piperazinyl]-2-oxoethyl]-  
 6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



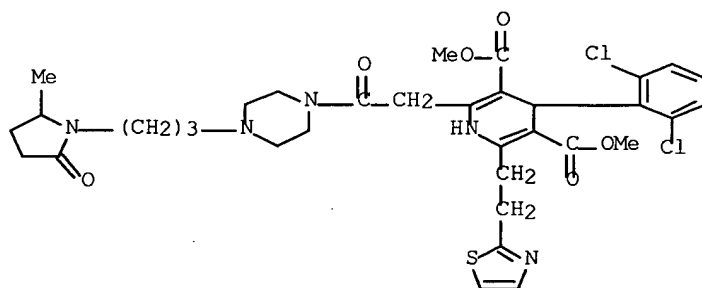
PAGE 1-A





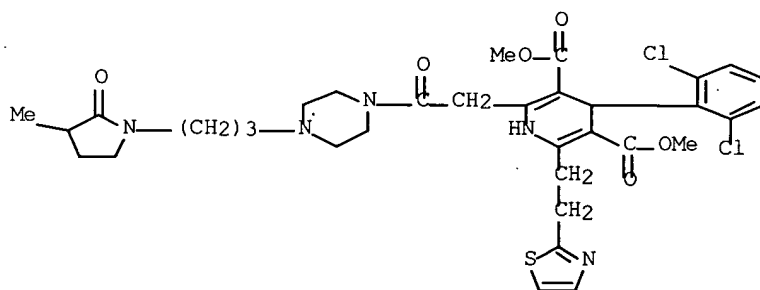
RN 344616-29-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[3-(2-methyl-5-oxo-1-pyrrolidinyl)propyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



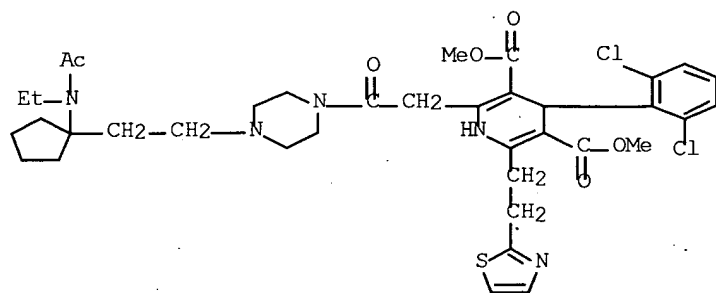
RN 344616-30-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[3-(3-methyl-2-oxo-1-pyrrolidinyl)propyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



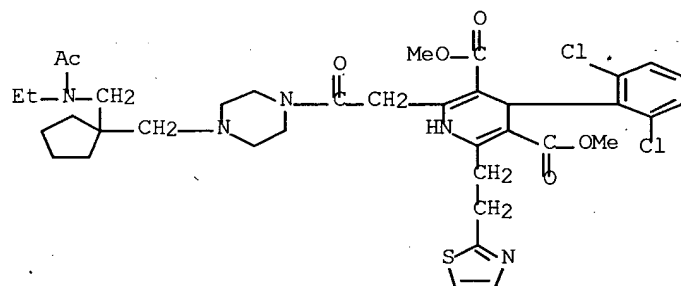
RN 344616-31-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[2-[1-(acetyethylamino)cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



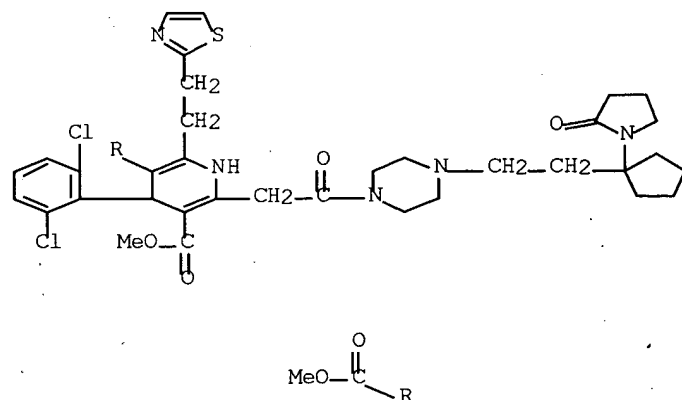
RN 344616-32-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-(acetyllethylamino)methyl]cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344616-33-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[2-[1-(2-oxo-1-pyrrolidinyl)cyclopentyl]ethyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

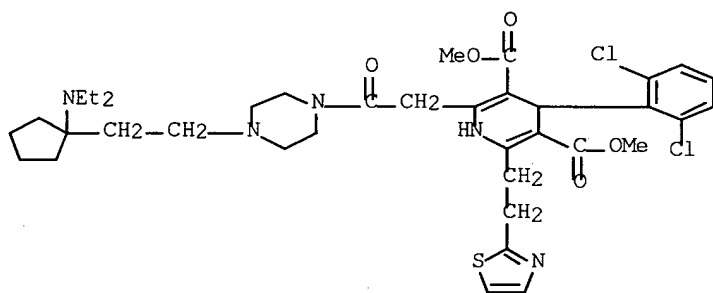


RN 344616-34-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[2-[1-(diethylamino)cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-1,4-

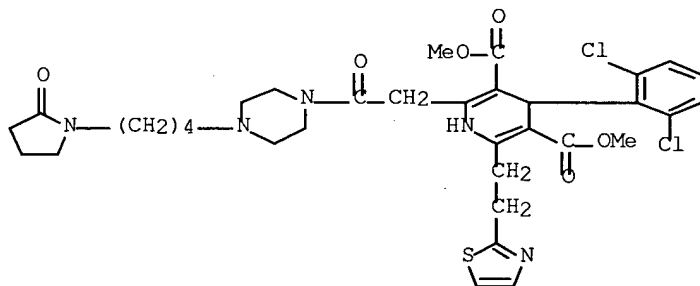
10/813,647

dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



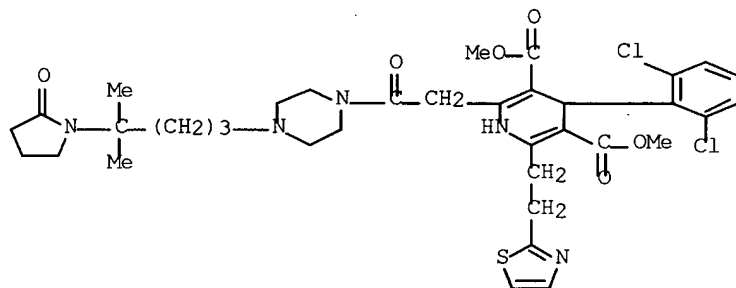
RN 344616-35-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[4-(2-oxo-1-pyrrolidinyl)butyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344616-36-0 HCAPLUS

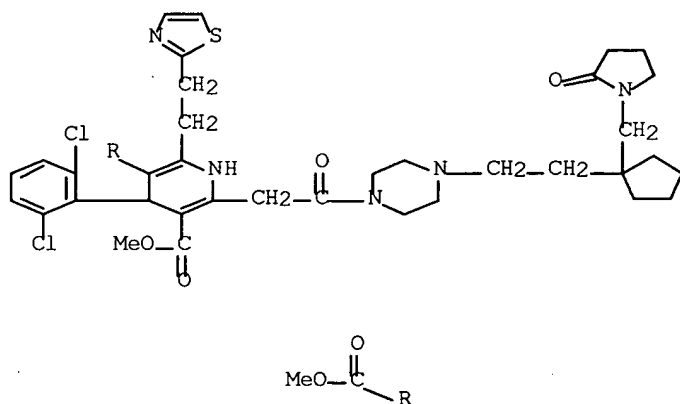
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[4-methyl-4-(2-oxo-1-pyrrolidinyl)pentyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344616-37-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[2-[1-[(2-oxo-1-pyrrolidinyl)methyl]cyclopentyl]ethyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester

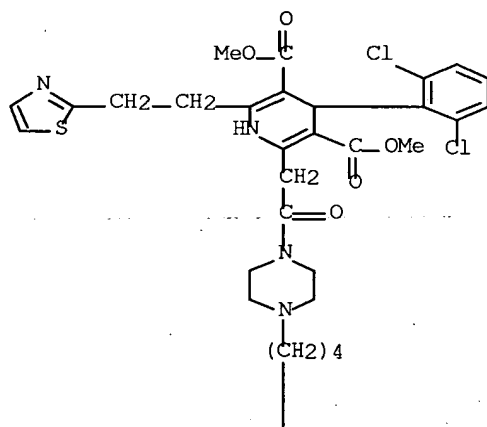
(9CI) (CA INDEX NAME)



RN 344616-38-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[4-(4-morpholinyl)butyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

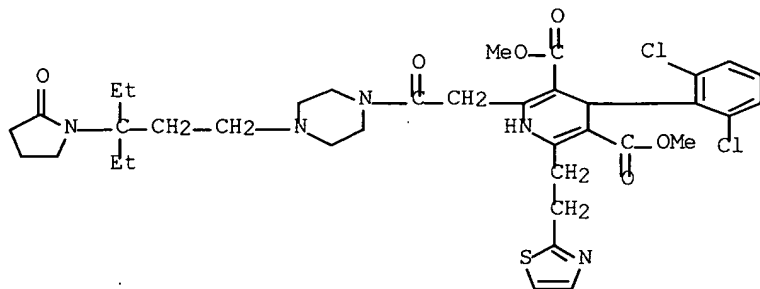


PAGE 2-A



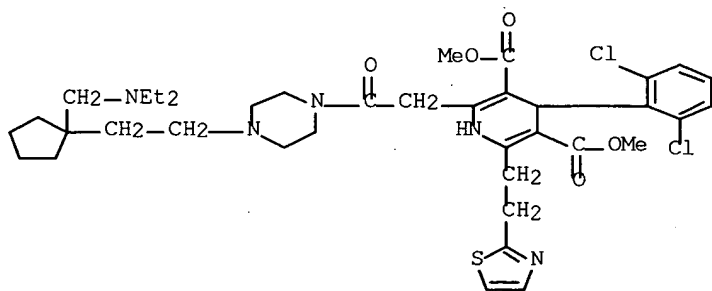
RN 344616-39-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-ethyl-3-(2-oxo-1-pyrrolidinyl)pentyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



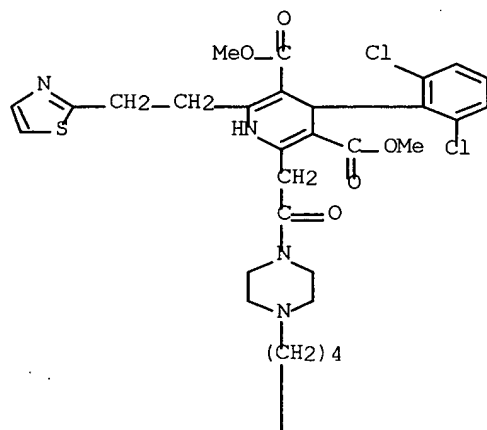
RN 344616-40-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[2-[1-[(diethylamino)methyl]cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



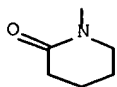
RN 344616-41-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[4-(2-oxo-1-piperidinyl)butyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



PAGE 1-A

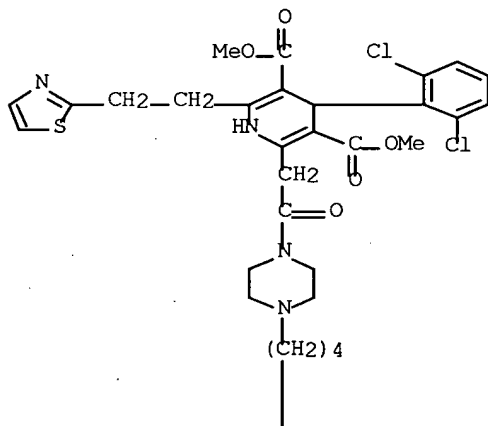
PAGE 2-A



RN 344616-42-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[4-(1-piperidinyl)butyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

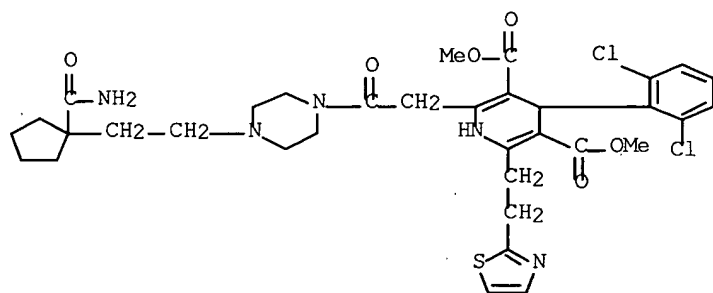


PAGE 2-A



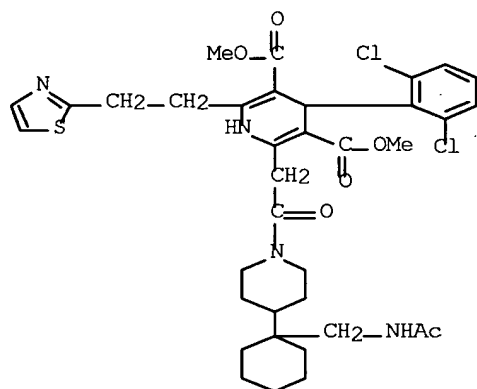
RN 344616-43-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[2-[1-(aminocarbonyl)cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



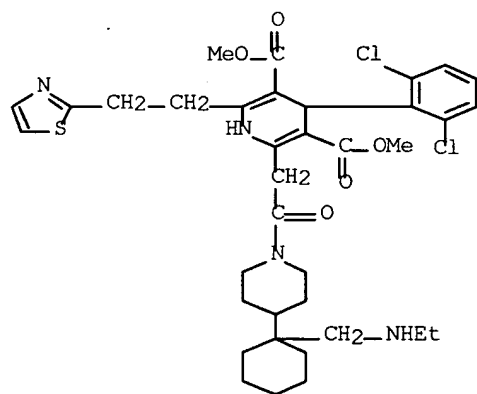
RN 344616-44-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[1-[(acetylamino)methyl]cyclohexyl]-1-piperidinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



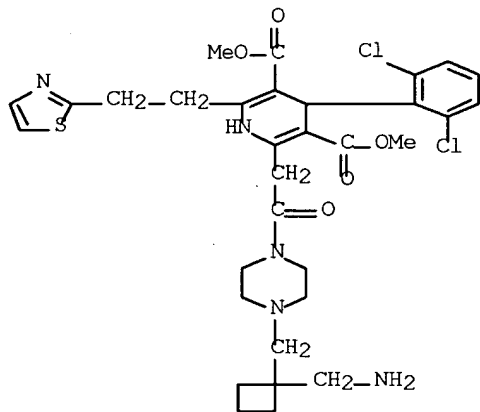
RN 344616-45-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[1-[(ethylamino)methyl]cyclohexyl]-1-piperidinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



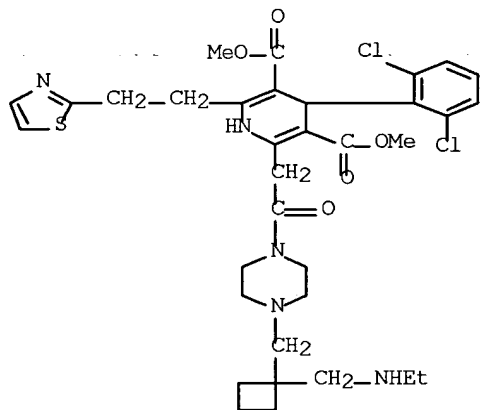
RN 344616-46-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-(aminomethyl)cyclobutyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344616-47-3 HCAPLUS

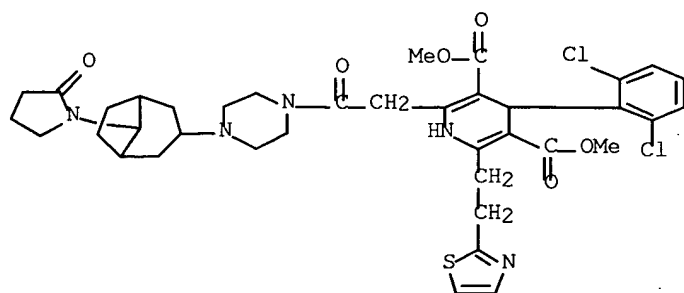
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-(ethylamino)methyl]cyclobutyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344616-48-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[8-(2-oxo-1-pyrrolidinyl)bicyclo[3.2.1]oct-3-yl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

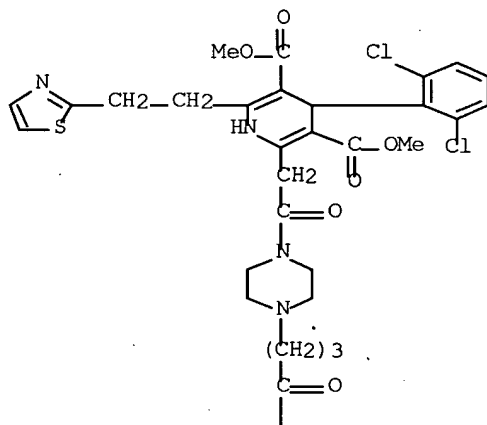




RN 344616-49-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[4-(4-morpholinyl)-4-oxobutyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

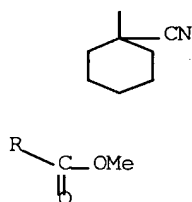
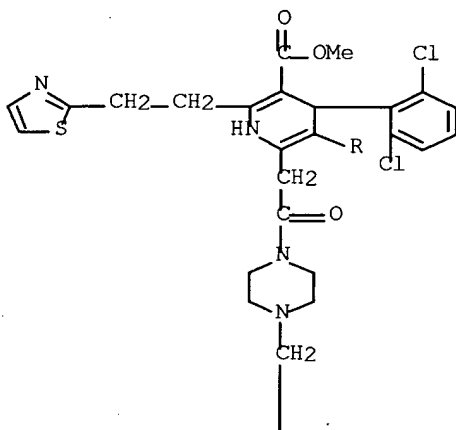


PAGE 2-A



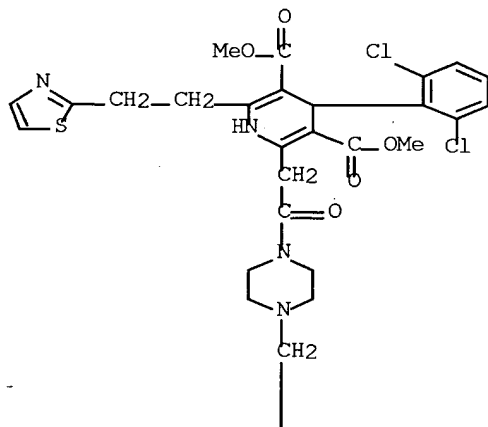
RN 344616-52-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[(1-cyanocyclohexyl)methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

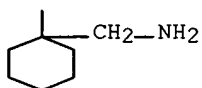


•x HCl

RN 344617-71-6 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-(aminomethyl)cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



PAGE 2-A

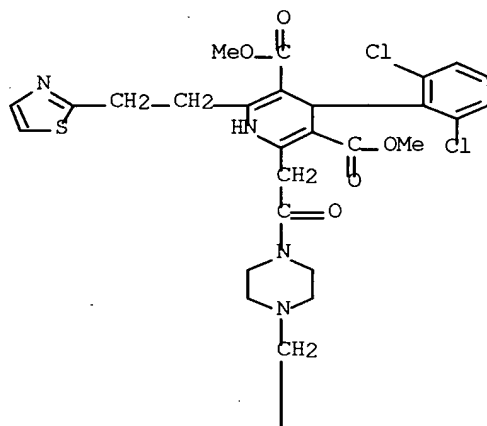


●2 HCl

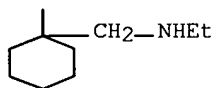
RN 344617-72-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-[(ethylamino)methyl]cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

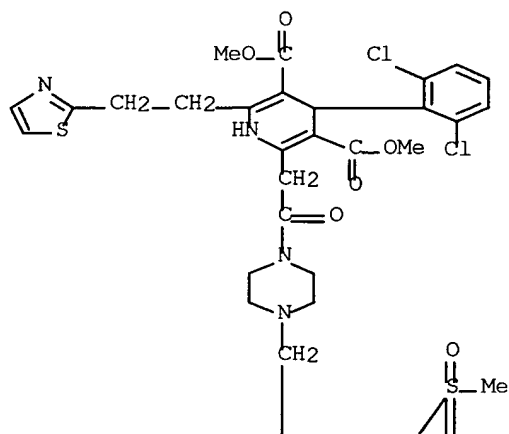


●x HCl

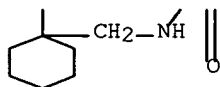
RN 344617-74-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[[1-[(methylsulfonyl)amino]methyl]cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

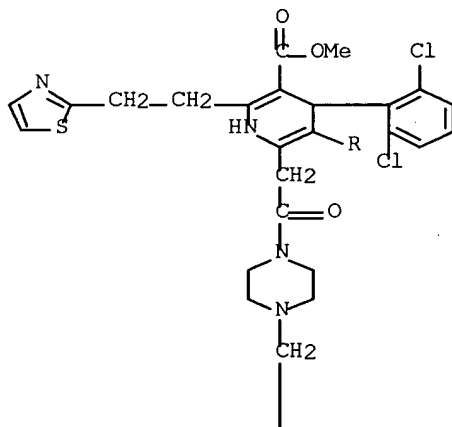


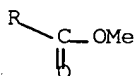
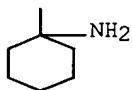
●x HCl

RN 344617-75-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[(1-aminocyclohexyl)methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

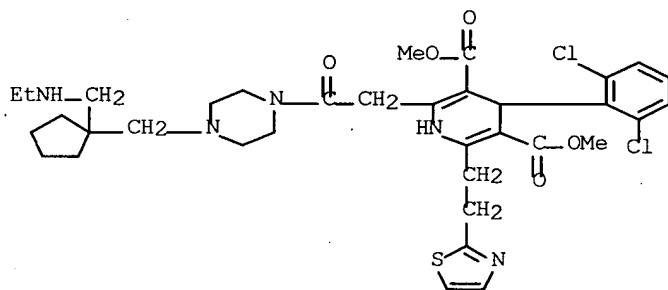




●x HCl

RN 344617-76-1 HCAPLUS

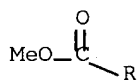
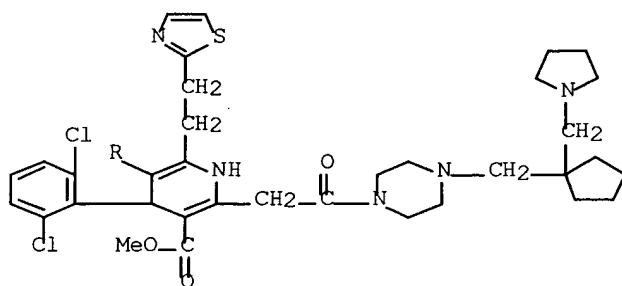
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-[(ethylamino)methyl]cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

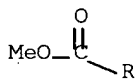
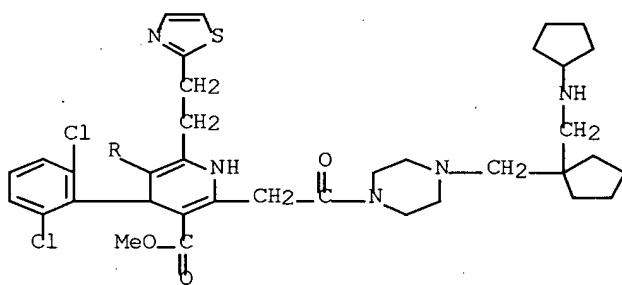
RN 344617-77-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[[1-(1-pyrrolidinylmethyl)cyclopentyl]methyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



•x HCl

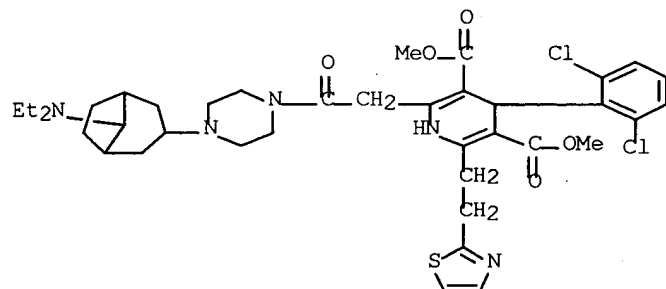
RN 344617-78-3 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-  
 [(cyclopentylamino)methyl]cyclopentyl]methyl]-1-piperazinyl]-2-  
 oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-  
 thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX  
 NAME)



•x HCl

RN 344617-79-4 HCAPLUS

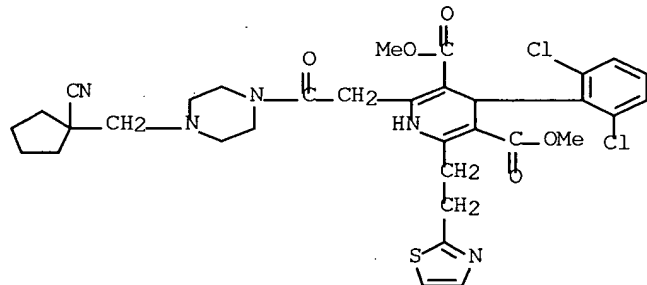
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[8-(diethylamino)bicyclo[3.2.1]oct-3-yl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 344617-80-7 HCAPLUS

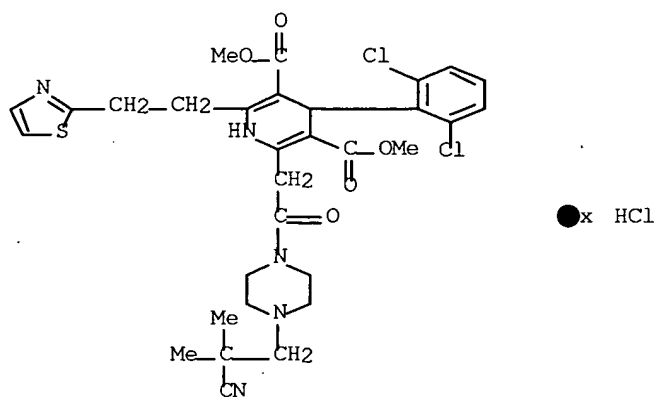
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[(1-cyanocyclopentyl)methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

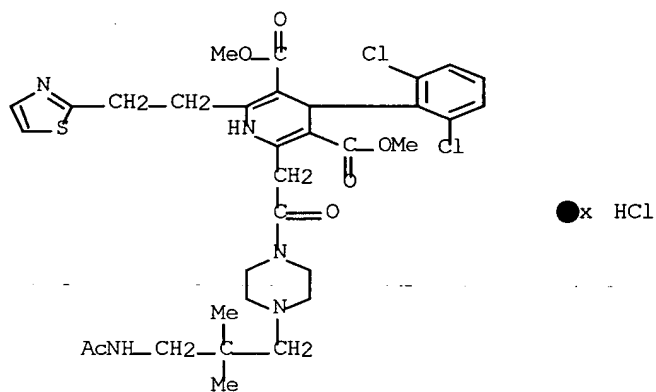
RN 344617-81-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(2-cyano-2-methylpropyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



RN 344617-82-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[3-(acetylamino)-2,2-dimethylpropyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

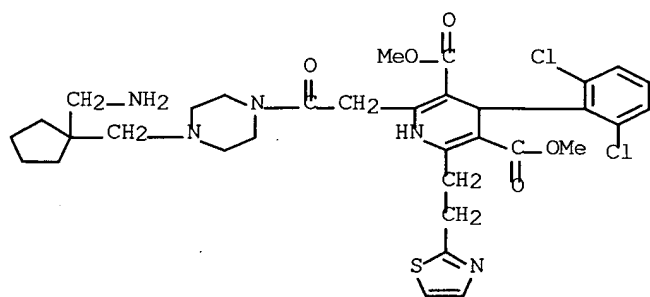


RN 344617-83-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[[1-(aminomethyl)cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



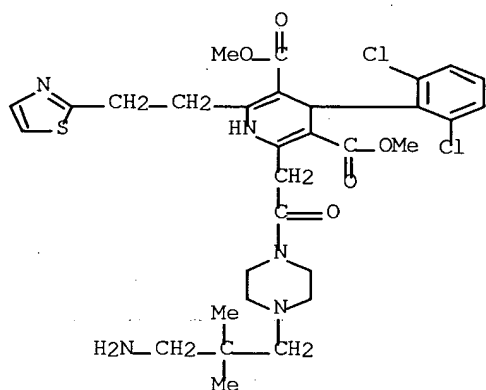
10/813,647



● x HCl

RN 344617-84-1 HCAPLUS

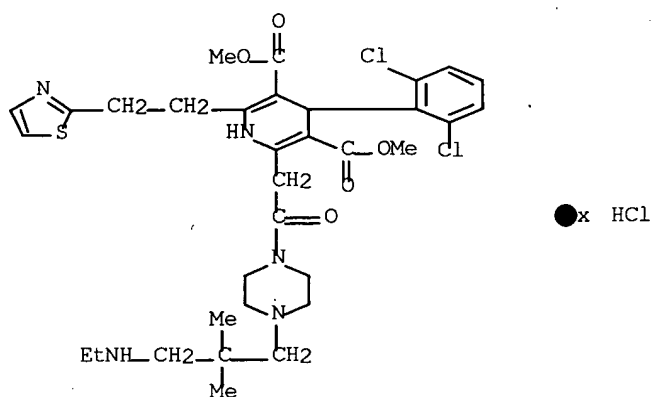
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3-amino-2,2-dimethylpropyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

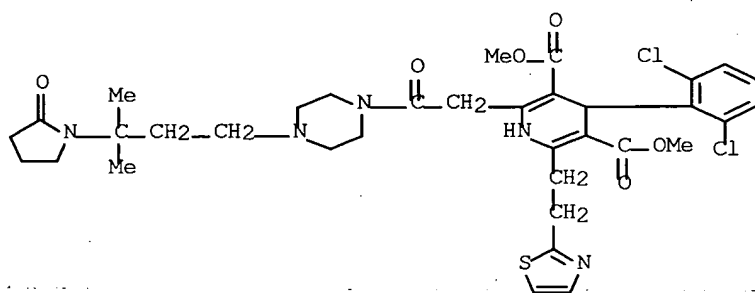
RN 344617-85-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-(ethylamino)-2,2-dimethylpropyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



RN 344617-86-3 HCAPLUS

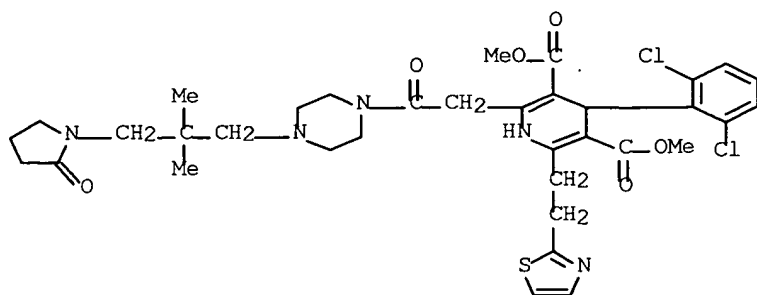
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[3-methyl-3-(2-oxo-1-pyrrolidinyl)butyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



RN 344617-87-4 HCAPLUS

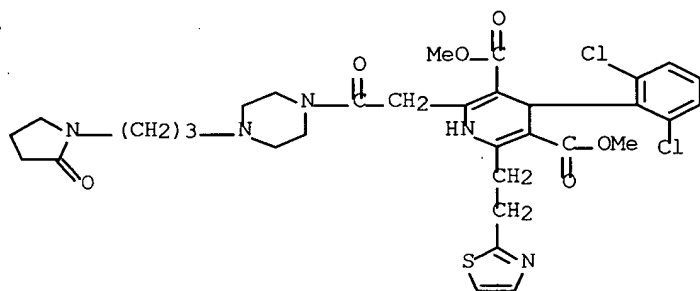
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[2,2-dimethyl-3-(2-oxo-1-pyrrolidinyl)propyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

10/813,647



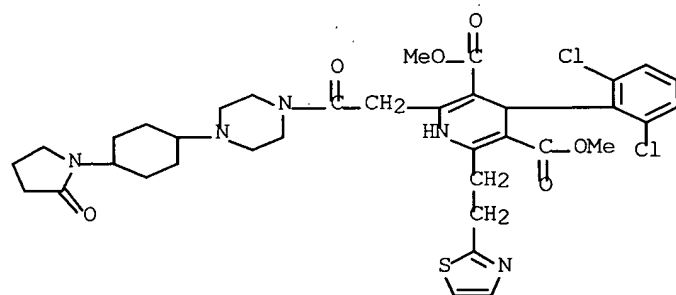
●x HCl

RN 344617-88-5 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[3-(2-oxo-1-pyrrolidinyl)propyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

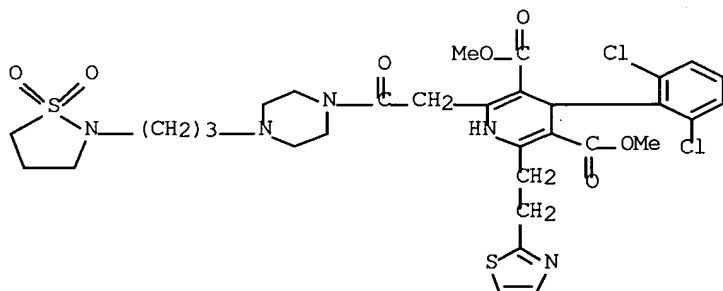
RN 344617-89-6 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[4-(2-oxo-1-pyrrolidinyl)cyclohexyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 344617-90-9 HCAPLUS

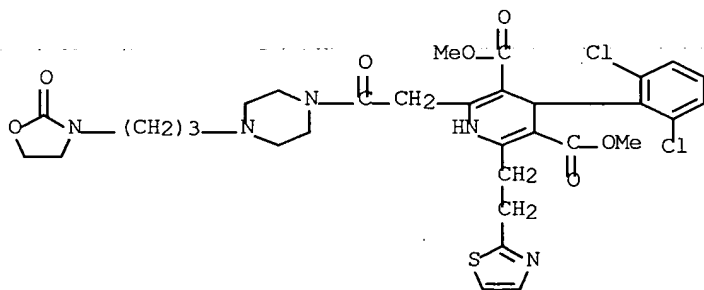
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-(1,1-dioxido-2-isothiazolidinyl)propyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 344617-91-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[3-(2-oxo-3-oxazolidinyl)propyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

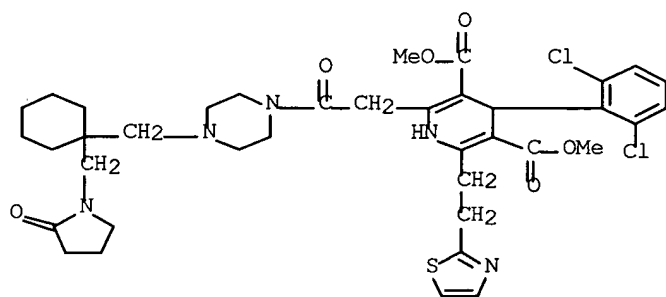


●x HCl

RN 344617-92-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[1-[(2-oxo-1-pyrrolidinyl)methyl]cyclohexyl]methyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

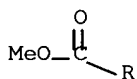
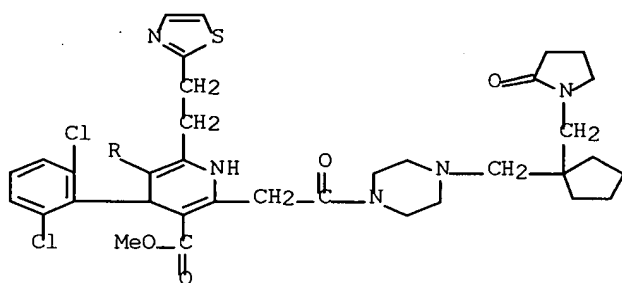
10/813,647



●x HCl

RN 344617-93-2 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[[1-[(2-oxo-1-pyrrolidinyl)methyl]cyclopentyl]methyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

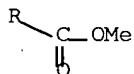
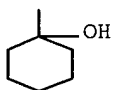
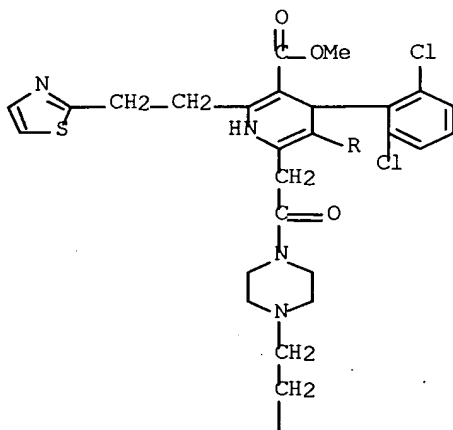
PAGE 1-A



PAGE 2-A

●x HCl

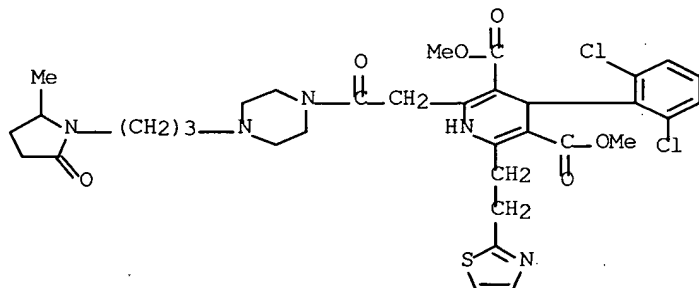
RN 344617-94-3 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[2-(1-hydroxycyclohexyl)ethyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 344617-95-4 HCAPLUS

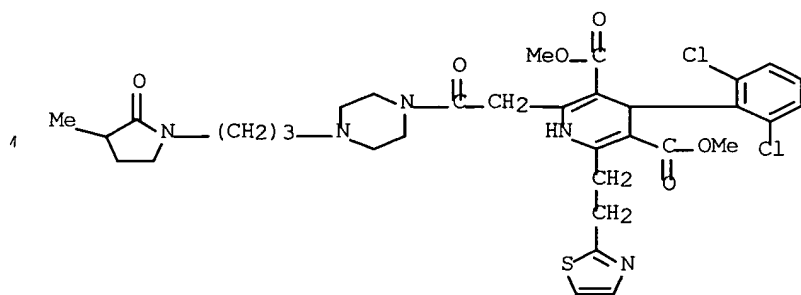
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[3-(2-methyl-5-oxo-1-pyrrolidinyl)propyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 344617-96-5 HCAPLUS

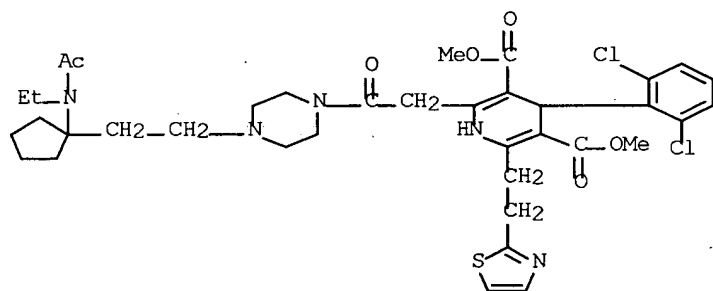
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[3-(3-methyl-2-oxo-1-pyrrolidiny)propyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 344617-97-6 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[2-[1-(acetyethylamino)cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

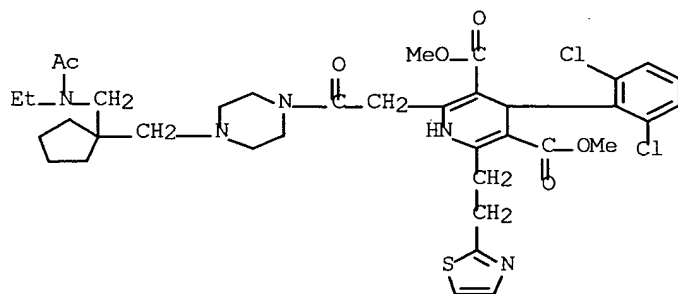


●x HCl

RN 344617-98-7 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[1-[(acetyethylamino)methyl]cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

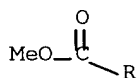
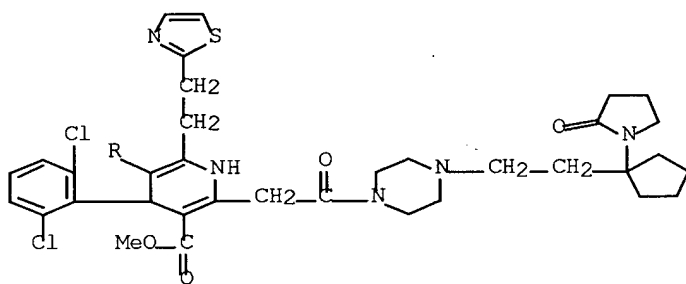
10/813,647



●x HCl

RN 344617-99-8 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[2-[1-(2-oxo-1-pyrrolidinyl)cyclopentyl]ethyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



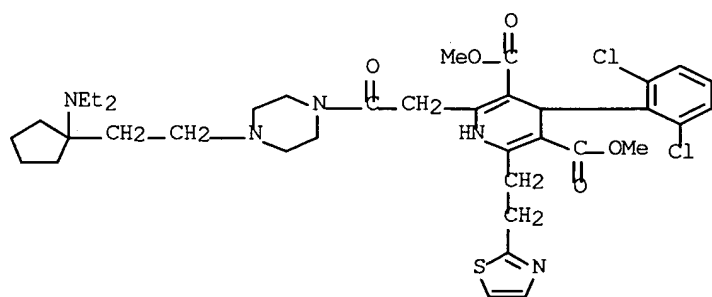
PAGE 2-A

●x HCl

RN 344618-00-4 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[2-[1-(diethylamino)cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



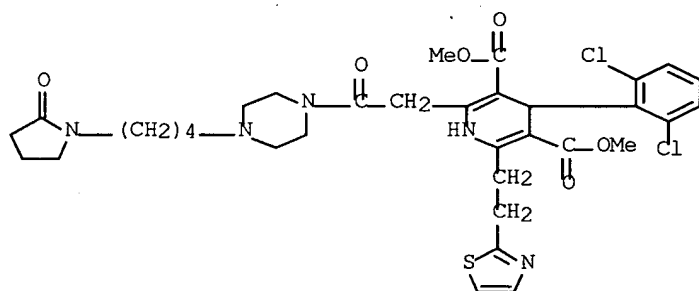
10/813,647



●x HCl

RN 344618-01-5 HCAPLUS

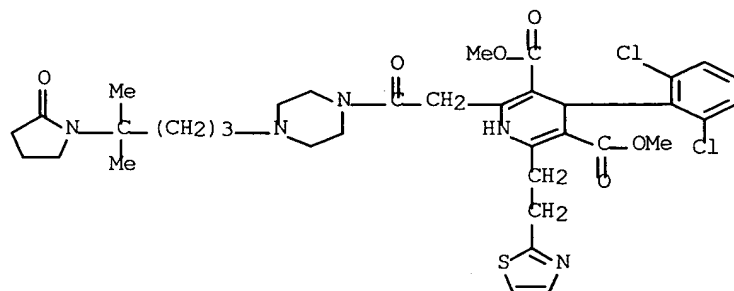
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[4-(2-oxo-1-pyrrolidinyl)butyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI)  
(CA INDEX NAME)



●x HCl

RN 344618-02-6 HCAPLUS

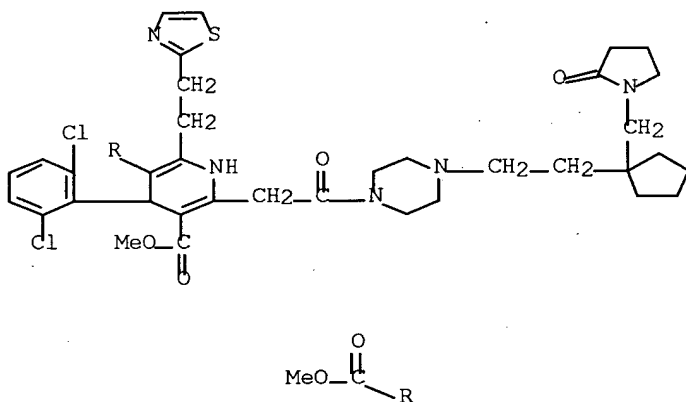
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[4-methyl-4-(2-oxo-1-pyrrolidinyl)pentyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI)  
(CA INDEX NAME)



●x HCl

RN 344618-03-7 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[2-[1-(2-oxo-1-pyrrolidinyl)methyl]cyclopentyl]ethyl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

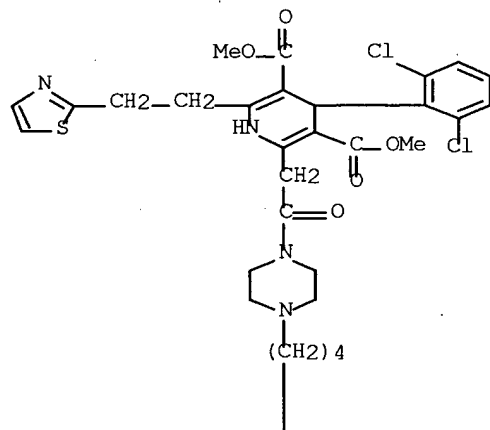


PAGE 2-A

● x HCl

RN 344618-04-8 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[4-(4-morpholinyl)butyl]-1-piperazinyl]-2-oxoethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

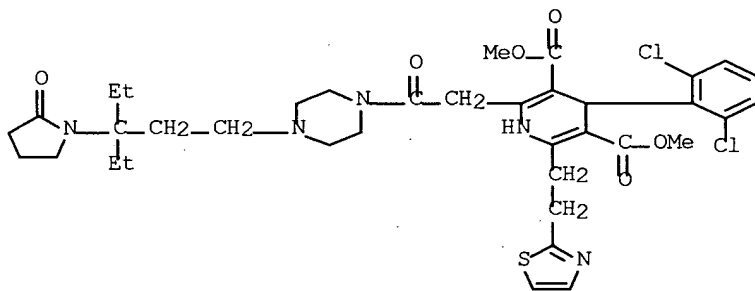




●x HCl

RN 344618-05-9 HCAPLUS

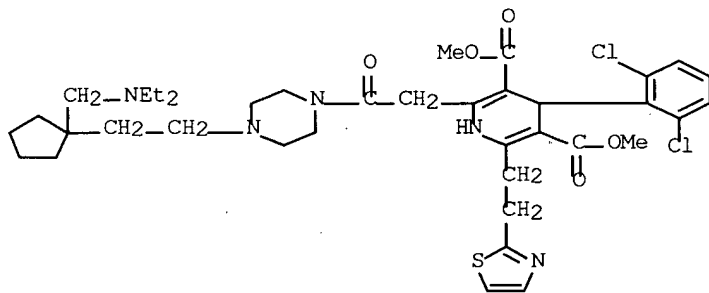
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-ethyl-3-(2-oxo-1-pyrrolidinyl)pentyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 344618-06-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[2-[1-[(diethylamino)methyl]cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

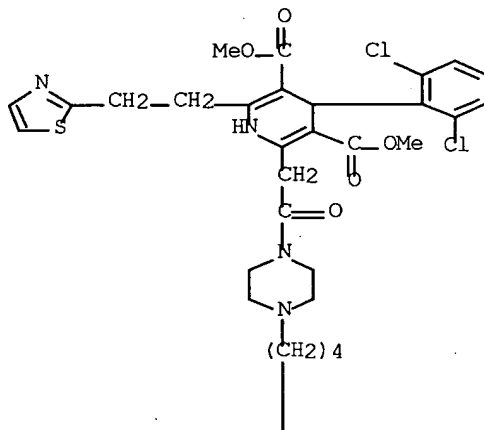


●x HCl

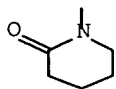
10/813,647

RN 344618-07-1 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-oxo-2-[4-[4-(2-oxo-1-piperidinyl)butyl]-1-piperazinyl]ethyl]-  
 6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI)  
 (CA INDEX NAME)

PAGE 1-A

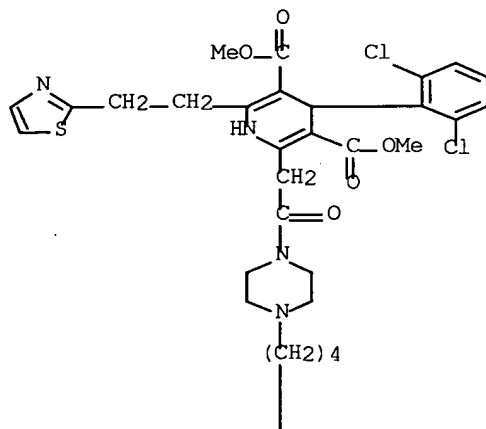


PAGE 2-A



●x HCl

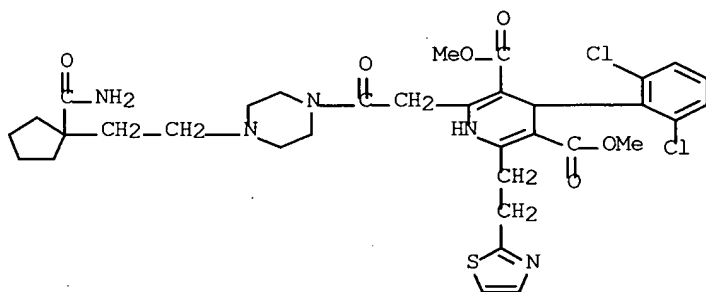
RN 344618-08-2 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-oxo-2-[4-[4-(1-piperidinyl)butyl]-1-piperazinyl]ethyl]-6-[2-  
 (2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA  
 INDEX NAME)



●x HCl

RN 344618-09-3 HCAPLUS

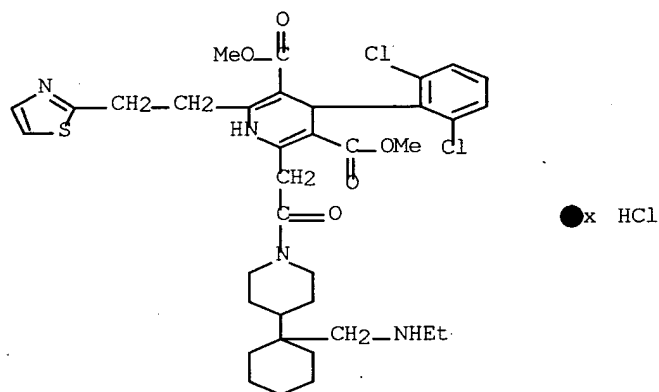
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[2-[1-(aminocarbonyl)cyclopentyl]ethyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



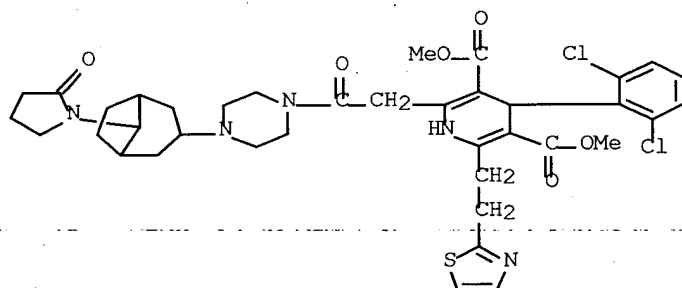
●x HCl

RN 344618-10-6 HCAPLUS

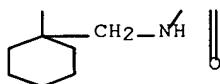
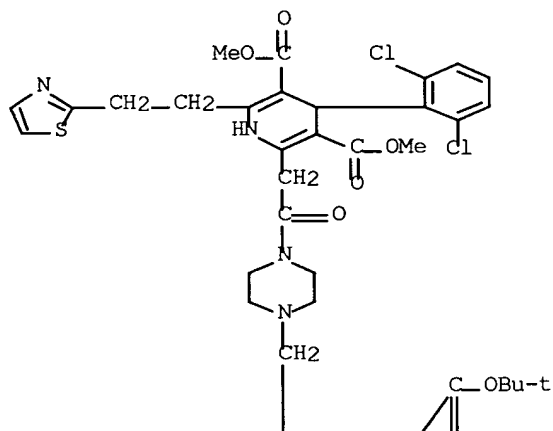
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[1-[(ethylamino)methyl]cyclohexyl]-1-piperidinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)



RN 344618-11-7 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[8-(2-oxo-1-pyrrolidinyl)bicyclo[3.2.1]oct-3-yl]-1-piperazinyl]ethyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, hydrochloride (9CI) (CA INDEX NAME)

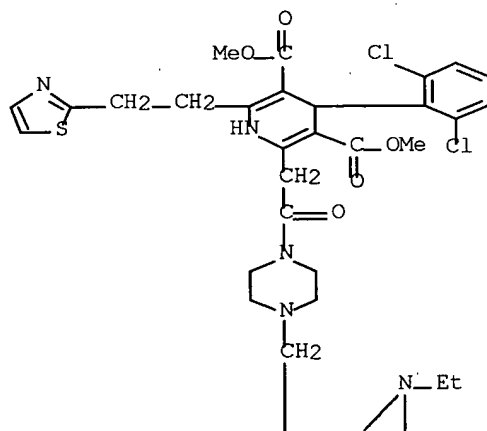


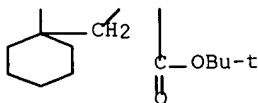
IT 344616-56-4P 344616-59-7P 344616-64-4P  
 344617-59-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation of 4-phenyl-2-thiazolylalkyl-1,4-dihydropyridine-3,5-dicarboxylates and analogs by reaction of benzylidenes with enamines as bradykinin antagonists)  
 RN 344616-56-4 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[[1-(1,1-dimethylethoxy)carbonyl]amino]methyl]cyclohexyl]methyl]-1-piperazinyl]-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344616-59-7 HCAPLUS

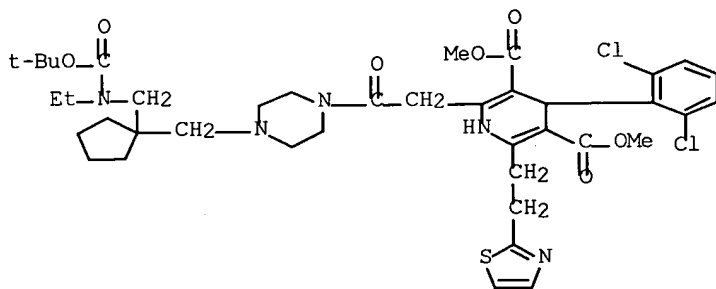
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-[[[(1,1-dimethylethoxy)carbonyl]ethylamino]methyl]cyclohexyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)





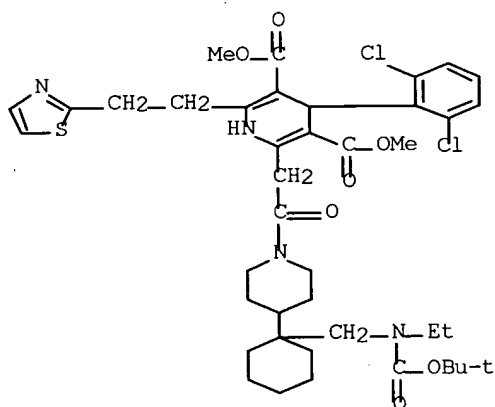
RN 344616-64-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[[1-[[[(1,1-dimethylethoxy)carbonyl]ethylamino]methyl]cyclopentyl]methyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 344617-59-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[1-[[[(1,1-dimethylethoxy)carbonyl]ethylamino]methyl]cyclohexyl]-1-piperidinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-thiazolyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IC ICM C07D417-06

ICS C07D417-12; C07D417-14; A61P009-00; A61K031-496

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

IT 344615-99-2P 344616-00-8P 344616-01-9P  
344616-02-0P 344616-03-1P 344616-04-2P  
344616-05-3P 344616-06-4P 344616-07-5P  
344616-08-6P 344616-09-7P 344616-10-0P



344616-11-1P 344616-12-2P 344616-13-3P  
 344616-15-5P 344616-16-6P 344616-17-7P  
 344616-19-9P 344616-20-2P 344616-21-3P  
 344616-22-4P 344616-23-5P 344616-24-6P  
 344616-25-7P 344616-26-8P 344616-27-9P  
 344616-28-0P 344616-29-1P 344616-30-4P  
 344616-31-5P 344616-32-6P 344616-33-7P  
 344616-34-8P 344616-35-9P 344616-36-0P  
 344616-37-1P 344616-38-2P 344616-39-3P  
 344616-40-6P 344616-41-7P 344616-42-8P  
 344616-43-9P 344616-44-0P 344616-45-1P  
 344616-46-2P 344616-47-3P 344616-48-4P  
 344616-49-5P 344616-52-0P 344617-71-6P  
 344617-72-7P 344617-74-9P 344617-75-0P  
 344617-76-1P 344617-77-2P 344617-78-3P  
 344617-79-4P 344617-80-7P 344617-81-8P  
 344617-82-9P 344617-83-0P 344617-84-1P  
 344617-85-2P 344617-86-3P 344617-87-4P  
 344617-88-5P 344617-89-6P 344617-90-9P  
 344617-91-0P 344617-92-1P 344617-93-2P  
 344617-94-3P 344617-95-4P 344617-96-5P  
 344617-97-6P 344617-98-7P 344617-99-8P  
 344618-00-4P 344618-01-5P 344618-02-6P  
 344618-03-7P 344618-04-8P 344618-05-9P  
 344618-06-0P 344618-07-1P 344618-08-2P  
 344618-09-3P 344618-10-6P 344618-11-7P

RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); SPN (Synthetic preparation);  
 THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)

(preparation of 4-phenyl-2-thiazolylalkyl-1,4-dihydropyridine-3,5-  
 dicarboxylates and analogs by reaction of benzylidenes with  
 enamines as bradykinin antagonists)

IT	134578-93-1P	184042-65-7P	195194-80-0P	198478-03-4P
	344434-91-9P	344434-93-1P	344434-95-3P	344434-97-5P
	344434-99-7P	344616-50-8P	344616-51-9P	344616-53-1P
	344616-54-2P	344616-55-3P	344616-56-4P	344616-57-5P
	344616-58-6P	344616-59-7P	344616-60-0P	344616-61-1P
	344616-62-2P	344616-63-3P	344616-64-4P	344616-65-5P
	344616-66-6P	344616-67-7P	344616-68-8P	344616-69-9P
	344616-70-2P	344616-71-3P	344616-72-4P	344616-73-5P
	344616-74-6P	344616-75-7P	344616-76-8P	344616-77-9P
	344616-78-0P	344616-79-1P	344616-80-4P	344616-81-5P
	344616-82-6P	344616-83-7P	344616-85-9P	344616-86-0P
	344616-87-1P	344616-88-2P	344616-89-3P	344616-90-6P
	344616-91-7P	344616-92-8P	344616-93-9P	344616-94-0P
	344616-95-1P	344616-96-2P	344616-97-3P	344616-98-4P
	344616-99-5P	344617-00-1P	344617-01-2P	344617-02-3P
	344617-03-4P	344617-04-5P	344617-05-6P	344617-06-7P
	344617-07-8P	344617-08-9P	344617-09-0P	344617-10-3P
	344617-11-4P	344617-12-5P	344617-13-6P	344617-14-7P
	344617-15-8P	344617-16-9P	344617-17-0P	344617-18-1P
	344617-19-2P	344617-22-7P	344617-25-0P	344617-28-3P
	344617-29-4P	344617-30-7P	344617-31-8P	344617-32-9P
	344617-33-0P	344617-34-1P	344617-35-2P	344617-36-3P
	344617-37-4P	344617-38-5P	344617-39-6P	344617-40-9P
	344617-41-0P	344617-42-1P	344617-43-2P	344617-44-3P
	344617-45-4P	344617-46-5P	344617-47-6P	344617-48-7P
	344617-49-8P	344617-50-1P	344617-51-2P	344617-52-3P
	344617-53-4P	344617-54-5P	344617-55-6P	344617-56-7P
	344617-57-8P	344617-58-9P	344617-59-0P	344617-60-3P
	344617-61-4P	344617-62-5P	344617-63-6P	344617-64-7P
	344617-65-8P	344617-66-9P	344617-67-0P	344617-68-1P
	344617-69-2P	344617-70-5P		

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)

(preparation of 4-phenyl-2-thiazolylalkyl-1,4-dihydropyridine-3,5-

dicarboxylates and analogs by reaction of benzylidenes with enamines as bradykinin antagonists)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:928 HCAPLUS Full-text

DOCUMENT NUMBER: 130:191795

TITLE: Inhibition of brain choline uptake by isoarecolone and lobeline derivatives: implications for potential vector-mediated brain drug delivery

AUTHOR(S): Metting, Traci L.; Burgio, David E.; Terry, Alvin V., Jr.; Beach, J. Warren; McCurdy, Chris R.; Allen, David D.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, School of Pharmacy, Amarillo, TX, 79106-1712, USA

SOURCE: Neuroscience Letters (1998), 258(1), 25-28

CODEN: NELED5; ISSN: 0304-3940

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Delivery of certain compds. to brain is restricted by the nature of the blood-brain barrier (BBB). Many valuable pharmaceuticals are excluded from the CNS due to hydrophilicity or charge. These limitations have been overcome by numerous methods. One method we use is to take advantage of saturable nutrient transporters located at the barrier. These systems transport hydrophilic and charged nutrients into brain such as choline, a quaternized neurotransmitter precursor. Using knowledge of their substrate specificity, it is possible to deliver agents into brain using these nutrient carriers. In this report, derivs. of lobeline and isoarecolone were evaluated to determine if they may gain access to brain by the blood-brain barrier basic amine transporter using the in situ brain perfusion technique. These compds. do bind the blood-brain barrier basic amine transporter and may enter brain by this transport system.

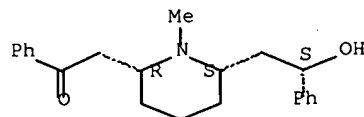
IT 90-69-7D, Lobeline, derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (inhibition of brain choline uptake by isoarecolone and lobeline derivs.: implications for potential vector-mediated brain drug delivery)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-11 (Pharmacology)

IT 90-69-7D, Lobeline, derivs. 115713-16-1D, Isoarecolone, derivs. 200572-47-0 220803-69-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (inhibition of brain choline uptake by isoarecolone and lobeline derivs.: implications for potential vector-mediated brain drug delivery)

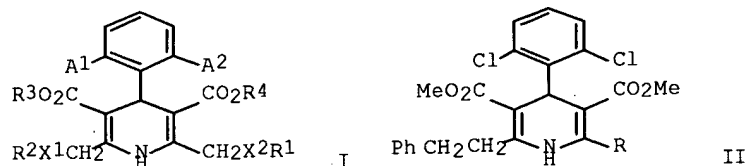
10/813,647

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L53 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1997:592266 HCAPLUS Full-text  
DOCUMENT NUMBER: 127:234256  
TITLE: Novel 4-phenyl-2-(aminoalkyl)-1,4-  
dihydropyridine-3,5-dicarboxylic acid  
derivatives as bradykinin receptor antagonists  
INVENTOR(S): Ikeda, Takafumi  
PATENT ASSIGNEE(S): Pfizer Inc., USA  
SOURCE: Eur. Pat. Appl., 23 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 790239	A1	19970820	EP 1997-200232	1997 0129
EP 790239	B1	20010912	<--	
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 205478	E	20010915	AT 1997-200232	1997 0129
ES 2162186	T3	20011216	ES 1997-200232	1997 0129
PT 790239	T	20020130	PT 1997-200232	1997 0129
US 5861402	A	19990119	US 1997-797681	1997 0131
JP 09227521	A2	19970902	JP 1997-42869	1997 0213
CA 2197739	AA	19970820	CA 1997-2197739	1997 0217
CA 2197739 GR 3037064	C T3	20000215 20020131	GR 2001-401936	2001 1030
PRIORITY APPLN. INFO.:			WO 1996-IB131	A 1996 0219
			EP 1997-200232	A 1997 0129
OTHER SOURCE(S):				

MARPAT 127:234256



AB Title compds. I [A1, A2= halo, H; X1 = CH2, CO, SO, SO2; X2 = CH2, CO; Y = aminoalkyl; R1 = morpholinoalkylphenyl, alkoxy carbonyl, acyl, dihydroimidazolyl, formamidino, guanidino, dihydroimidazolylamino, H, alkyl, piperidiny, cycloalkyl, bicycloalkyl, tricycloalkyl, azacyclo-, azabicyclo-, azatricycloalkyl, bicycloalkenyl, benzocycloalkyl, heterocyclic] were prepared and have excellent bradykinin antagonistic activity. Thus, the dihydropyridine II [R = CH2CO2Me] was methylated, treated with N-methylpiperazine, and deacboxylated to give II [R = 2-(4-methylpiperazino)ethyl]. Various I had IC50 of 10Nm - 1µM for inhibition of [3H]bradykinin binding at its receptor.

IT 195145-32-5P 195145-34-7P 195145-36-9P  
195145-38-1P 195145-57-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

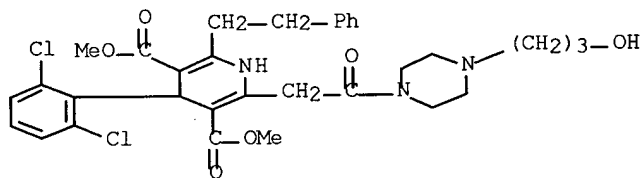
```

separation), KAC1 (Reactant or Reagent,
(preparation of arylidihydropyridinedicarboxylates as bradykinin
receptor antagonists)

```

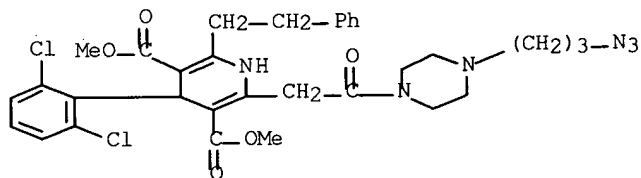
RN 195145-32-5 HCAPLUS

3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
2-[2-[4-(3-hydroxypropyl)-1-piperazinyl]-2-oxoethyl]-6-(2-  
phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



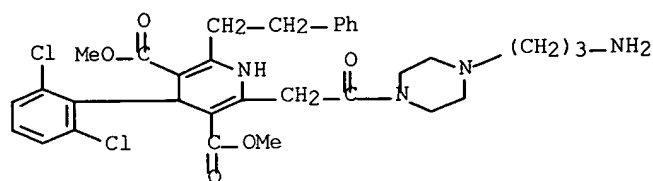
RN 195145-34-7 HCAPLUS

3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3-azidopropyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



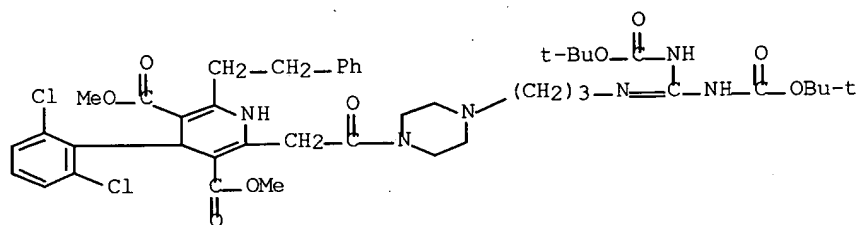
RN 195145-36-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3-aminopropyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



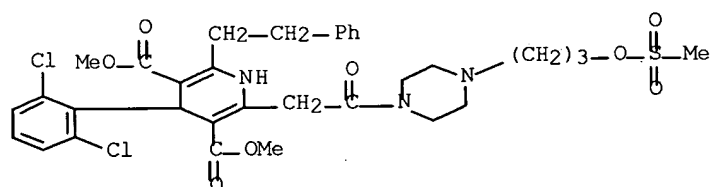
RN 195145-38-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[3-[[bis[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]propyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



RN 195145-57-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-[3-[(methylsulfonyl)oxy]propyl]-1-piperazinyl]-2-oxoethyl]-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



IT 195145-31-4P 195145-37-0P 195145-39-2P

195145-40-5P 195145-41-6P 195145-43-8P

195145-44-9P 195145-47-2P 195145-49-4P

195145-51-8P 195145-55-2P 195145-56-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

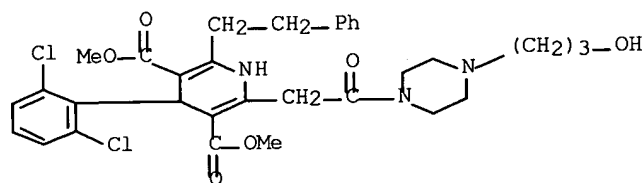
(preparation of aryldihydropyridinedicarboxylates as bradykinin receptor antagonists)

RN 195145-31-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-

10/813,647

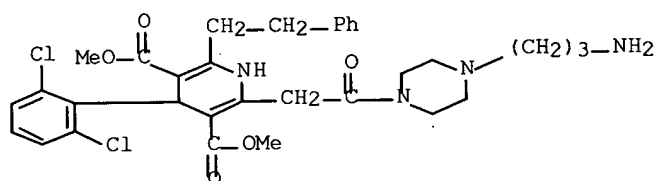
2-[2-[4-(3-hydroxypropyl)-1-piperazinyl]-2-oxoethyl]-6-(2-phenylethyl)-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 195145-37-0 HCAPLUS

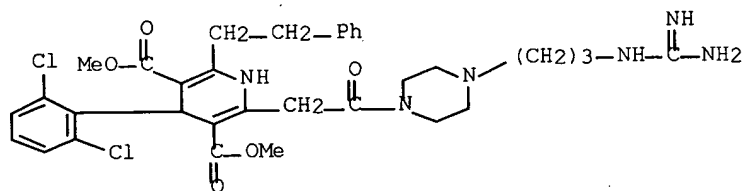
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(3-aminopropyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 195145-39-2 HCAPLUS

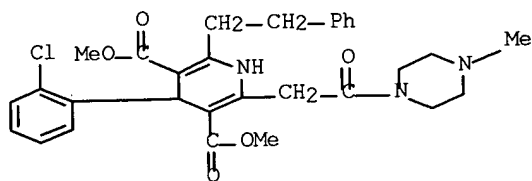
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[3-[(aminoiminomethyl)amino]propyl]-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



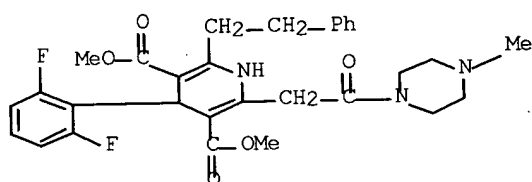
●2 HCl

RN 195145-40-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2-chlorophenyl)-1,4-dihydro-2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



RN 195145-41-6 HCAPLUS  
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-difluorophenyl)-1,4-dihydro-  
2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-(2-phenylethyl)-,  
dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

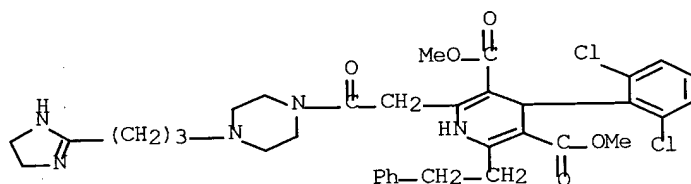


● HCl

```

RN      195145-43-8   HCAPLUS
CN      3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-
      (4,5-dihydro-1H-imidazol-2-yl)propyl]-1-piperazinyl]-2-oxoethyl]-
      1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester, monohydriodide
      monohydrochloride (9CI) (CA INDEX NAME)

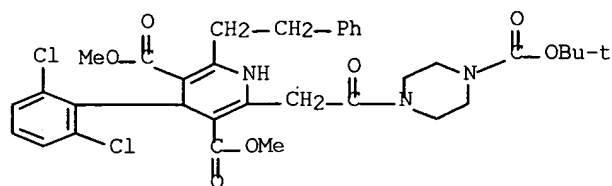
```



● HCl

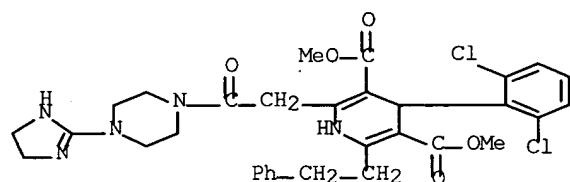
● HI

RN	195145-44-9	HCAPLUS
CN	3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(1,1-dimethylethoxy)carbonyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)	



RN 195145-47-2 HCAPLUS

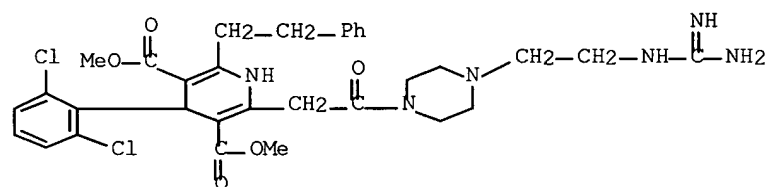
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-(4,5-dihydro-1H-imidazol-2-yl)-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester, monohydriodide (9CI) (CA INDEX NAME)



● HI

RN 195145-49-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-[2-(2-phenylethyl)-1,4-dihydro-6-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

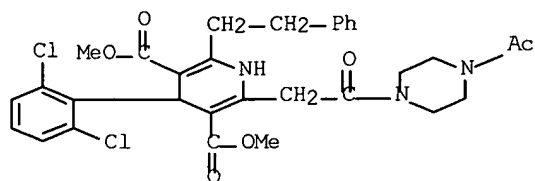


●2 HCl

RN 195145-51-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-(4-acetyl-1-piperazinyl)-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

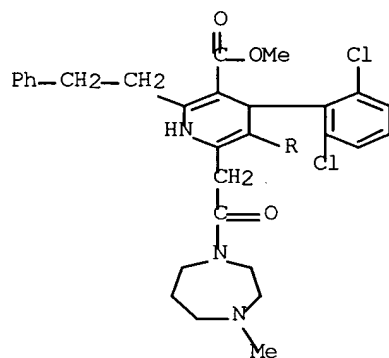




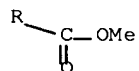
RN 195145-55-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-2-oxoethyl]-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

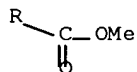
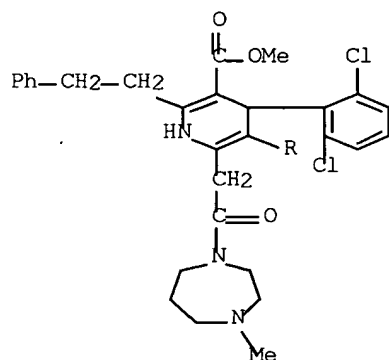


PAGE 2-A



RN 195145-56-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-2-oxoethyl]-1,4-dihydro-6-(2-phenylethyl)-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IC ICM C07D211-90  
ICS C07D401-12; C07D453-02; C07D451-02  
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1  
IT 6425-46-3P 51013-67-3P, 4-Morpholinomethylaniline 63547-62-6P  
178377-49-6P 178377-50-9P 195145-26-7P 195145-27-8P  
**195145-32-5P 195145-34-7P 195145-36-9P**  
**195145-38-1P 195145-57-4P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation of aryldihydropyridinedicarboxylates as bradykinin  
receptor antagonists)  
IT 195145-28-9P 195145-30-3P **195145-31-4P**  
**195145-37-0P 195145-39-2P 195145-40-5P**  
**195145-41-6P 195145-42-7P 195145-43-8P**  
**195145-44-9P 195145-45-0P 195145-47-2P**  
195145-48-3P **195145-49-4P** 195145-50-7P  
**195145-51-8P 195145-52-9P 195145-53-0P 195145-54-1P**  
**195145-55-2P 195145-56-3P**  
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**;  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of aryldihydropyridinedicarboxylates as bradykinin  
receptor antagonists)

L53 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1997:587253 HCAPLUS Full-text  
DOCUMENT NUMBER: 127:248125  
TITLE: Preparation of 2-(piperazinylcarbonylmethyl)-  
3,5-bis(methoxycarbonyl)-1,4-dihydropyridines  
as bradykinin antagonists.  
INVENTOR(S): Ikeda, Takafumi  
PATENT ASSIGNEE(S): Pfizer Pharmaceuticals Inc., Japan; Pfizer  
Inc.  
SOURCE: PCT Int. Appl., 42 pp.

10/813,647

DOCUMENT TYPE: CODEN: PIXXD2  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: English  
 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730048	A1	19970821	WO 1997-IB58	1997 0127
<--				
W: AU, BG, BR, BY, CA, CN, CZ, HU, IL, IS, JP, KR, KZ, LK, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9713964	A1	19970902	AU 1997-13964	1997 0127
<--				
EP 882044	A1	19981209	EP 1997-900401	1997 0127
<--				
EP 882044	B1	20020717		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI				
CN 1211251	A	19990317	CN 1997-192240	1997 0127
<--				
JP 11507949	T2	19990713	JP 1997-529138	1997 0127
<--				
JP 3167335	B2	20010521		
BR 9707568	A	19990727	BR 1997-7568	1997 0127
<--				
AT 220676	E	20020815	AT 1997-900401	1997 0127
<--				
CA 2245857	C	20021001	CA 1997-2245857	1997 0127
<--				
CA 2245857	AA	19970821		
PT 882044	T	20021129	PT 1997-900401	1997 0127
<--				
ES 2177921	T3	20021216	ES 1997-900401	1997 0127
<--				
ZA 9701357	A	19980818	ZA 1997-1357	1997 0218
<--				
NO 9803776	A	19980818	NO 1998-3776	1998 0818
<--				

10/813,647

US 6131226

A

20001017

US 1999-125137

1999

0201

PRIORITY APPLN. INFO.:

&lt;--

WO 1996-IB132

A

1996

0219

&lt;--

WO 1997-IB58

W

1997

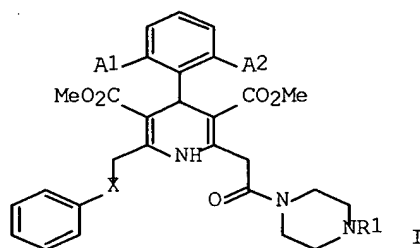
0127

&lt;--

OTHER SOURCE(S):

MARPAT 127:248125

GI



AB Title compds. [I; A1, A2 = halo; X = CO, SO<sub>2</sub>, SO(CH<sub>2</sub>)<sub>n</sub>; n = 0-2; R1 = 8-azabicyclo[3.2.1]octyl, quinuclidinyl, bicyclo[3.3.0]octyl, cycloalkyl, 2,3,5,6-tetrahydro-4H-thiopyranyl, (substituted) cycloalkylalkyl], were prepared I have excellent bradykinin antagonistic activity and are useful for the treatment of inflammation, cardiovascular disease, pain, common cold, allergies, asthma, pancreatitis, burns, virus infection, head injury, or multiple trauma. Thus, Me 2-(4,6-dichlorophenylmethylidene)-3-oxo-4-phenylthiobutanoate (preparation given) and di-Me 3-aminoglutaconate were heated at 120° for 3 h to give 40.6% di-Me 4-(2,6-dichlorophenyl)-2-methoxycarbonylmethyl-6-phenylthiomethyl-1,4-dihydropyridine-3,5-dicarboxylate. This was oxidized to the phenylsulfinyl derivative, which was partially saponified followed by amidation with 1-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)piperazine using N-1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in CH<sub>2</sub>Cl<sub>2</sub> to give di-Me 4-(2,6-dichlorophenyl)-2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]carbonylmethyl-6-phenylsulfinylmethyl-1,4-dihydropyridine-3,5-dicarboxylate dihydrochloride. I inhibited [3H]bradykinin binding to ileum preps. with IC<sub>50</sub> = 0.2-10 nM.

IT 195503-94-7P 195503-95-8P 195503-96-9P

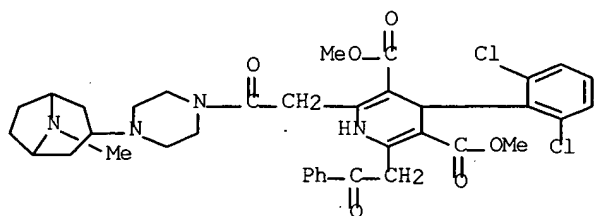
195504-30-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-(piperazinylcarbonylmethyl)-3,5-bis(methoxycarbonyl)-1,4-dihydropyridines as bradykinin antagonists)

RN 195503-94-7 HCAPLUS

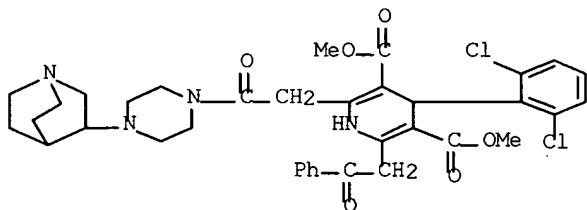
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-6-(2-oxo-2-phenylethyl)-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 195503-95-8 HCAPLUS

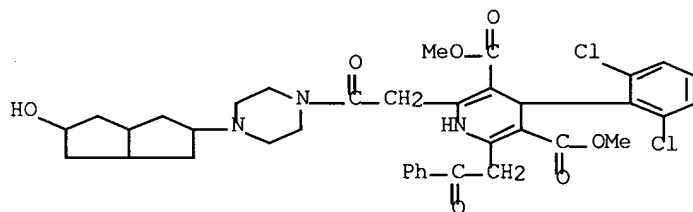
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(1-azabicyclo[2.2.2]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-(2-oxo-2-phenylethyl)-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 195503-96-9 HCAPLUS

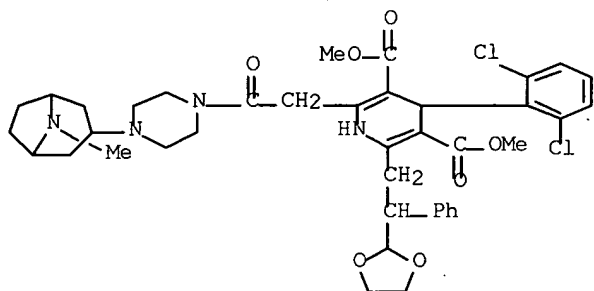
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(octahydro-5-hydroxy-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-6-(2-oxo-2-phenylethyl)-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 195504-30-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-(1,3-dioxolan-2-yl)-2-phenylethyl]-1,4-dihydro-6-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

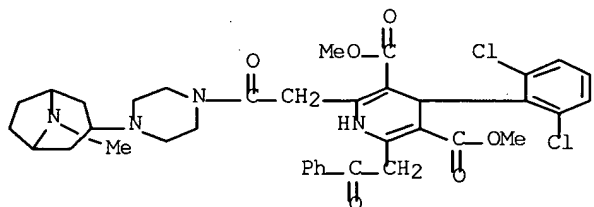


IT 195504-05-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation of 2-(piperazinylcarbonylmethyl)-3,5-  
bis(methoxycarbonyl)-1,4-dihydropyridines as bradykinin  
antagonists)

RN 195504-05-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
2-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-  
oxoethyl]-6-(2-oxo-2-phenylethyl)-, dimethyl ester (9CI) (CA  
INDEX NAME)



IC ICM C07D451-04

ICS A61K031-445; C07D453-02; C07D211-90; C07D405-12; C07D409-12

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT 195503-93-6P 195503-94-7P 195503-95-8P

195503-96-9P 195503-97-0P 195503-98-1P 195503-99-2P

195504-00-8P 195504-01-9P 195504-02-0P 195504-03-1P

195504-12-2P 195504-13-3P 195504-14-4P 195504-15-5P

195504-16-6P 195504-17-7P 195504-18-8P 195504-19-9P

195504-20-2P 195504-21-3P 195504-22-4P 195504-23-5P

195504-24-6P 195504-25-7P 195504-26-8P 195504-27-9P

195504-30-4P 195504-31-5P

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); SPN (Synthetic preparation);  
THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(preparation of 2-(piperazinylcarbonylmethyl)-3,5-  
bis(methoxycarbonyl)-1,4-dihydropyridines as bradykinin  
antagonists)

IT 51849-20-8P 63547-62-6P 178377-64-5P 178377-65-6P

178377-70-3P 178377-71-4P 195504-04-2P 195504-05-3P

195504-06-4P 195504-07-5P 195504-08-6P 195504-09-7P

195504-10-0P 195504-11-1P 195504-28-0P 195504-29-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)

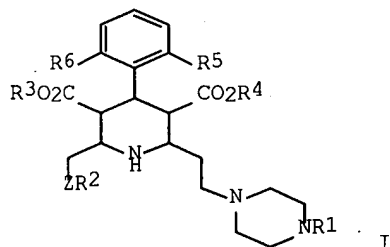
(preparation of 2-(piperazinylcarbonylmethyl)-3,5-

bis(methoxycarbonyl)-1,4-dihydropyridines as bradykinin antagonists)

L53 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:404662 HCAPLUS Full-text  
 DOCUMENT NUMBER: 125:86676  
 TITLE: Preparation of 2-(piperazinocarbonylmethyl)-  
 1,4-dihydropyridinedicarboxylates as  
 bradykinin antagonists  
 INVENTOR(S): Ito, Fumitaka; Kondo, Hiroshi; Hageman, David  
 L.; Lowe, John A., III; Nakanishi, Susumu;  
 Vinick, Fredric J.  
 PATENT ASSIGNEE(S): Pfizer Pharmaceuticals Inc., Japan  
 SOURCE: PCT Int. Appl., 64 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606083	A1	19960229	WO 1994-JP1398	1994 0824
<--				
W: JP CA 2198231	AA	19960229	CA 1995-2198231	1995 0526
<--				
CA 2198231 WO 9606082	C A1	19991207 19960229	WO 1995-IB400	1995 0526
<--				
W: AU, CA, CN, FI, JP, KR, MX, NO, NZ, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE	A1	19960314	AU 1995-24166	1995 0526
<--				
AU 689587 EP 777653	B2 A1	19980402 19970611	EP 1995-918113	1995 0526
<--				
EP 777653 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE	B1 A	20010822 19970806	CN 1995-194758	1995 0526
<--				
CN 1087737 JP 09510992	B T2	20020717 19971104	JP 1996-507896	1995 0526
<--				
JP 3001978 AT 204567	B2 E	20000124 20010915	AT 1995-918113	1995 0526
<--				
ES 2159637	T3	20011016	ES 1995-918113	

				1995 0526
PT 777653	T	20020228	PT 1995-918113	
				1995 0526
TW 500722	B	20020901	TW 1995-84107170	
				1995 0711
IL 114968	A1	19990817	IL 1995-114968	
				1995 0817
ZA 9707057	A	19970224	ZA 1997-7057	
				1995 0823
FI 9700745	A	19970221	FI 1997-745	
				1997 0221
NO 9700806	A	19970421	NO 1997-806	
				1997 0221
US 5859011	A	19990112	US 1997-793561	
				1997 0701
GR 3036907	T3	20020131	GR 2001-401777	
				2001 1016
PRIORITY APPLN. INFO.:			WO 1994-JP1398	A
				1994 0824
			EP 1995-918113	A
				1995 0526
			WO 1995-IB400	W
				1995 0526
OTHER SOURCE(S):				
GI				
MARPAT 125:86676				





AB Title compds. [I; R1 = H, (un)substituted (cyclo)alkyl, azacycloalkyl, etc.; R2 = H, alkyl, Ph, etc.; R3,R4 = alkyl; R5,R6 = halo; Z = bond, CH2, O, CO, etc.] were prepared Thus, 2,6-Cl2C6H3CH:C(CO2Me)COCH2CH2Ph was cyclocondensed with MeO2CCH:C(NH2)CO2Me (preparation each given) and the product amidated by N-methylpiperazine to give I (R1 = R3 = R4 = Me, R2 = Ph, R5 = R6 = Cl, Z = CH2). I had IC50 of 5nM to 1µM against bradykinin binding at ileum tissue preparation in vitro.

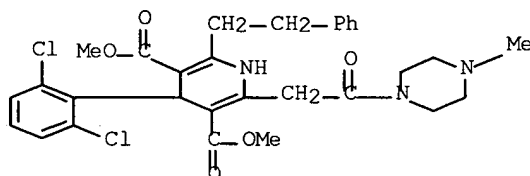
IT 178376-98-2P 178377-26-9P 178377-27-0P  
 178377-28-1P 178377-29-2P 178377-30-5P  
 178377-31-6P 178377-32-7P 178377-33-8P  
 178377-34-9P 178377-35-0P 178377-36-1P  
 178377-37-2P 178377-38-3P 178377-39-4P  
 178377-40-7P 178377-41-8P 178377-42-9P  
 178377-43-0P 178377-44-1P 178377-45-2P  
 178377-46-3P 178377-47-4P 178377-48-5P  
 178377-82-7P 178377-83-8P 178377-84-9P  
 178377-85-0P 178377-86-1P 178377-87-2P  
 178377-88-3P 178377-89-4P 178377-90-7P  
 178377-91-8P 178377-92-9P 178377-93-0P  
 178377-94-1P 178377-95-2P 178377-96-3P  
 178377-97-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-(piperazinocarbonylmethyl)-1,4-dihydropyridinedicarboxylates as bradykinin antagonists)

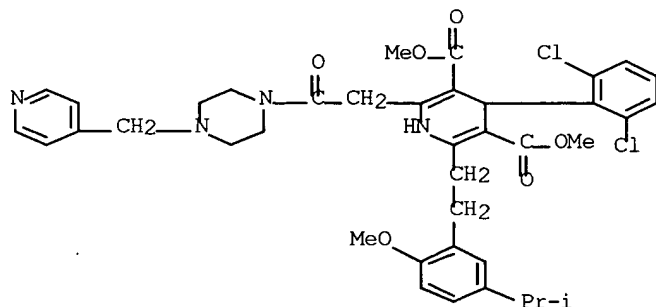
RN 178376-98-2 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

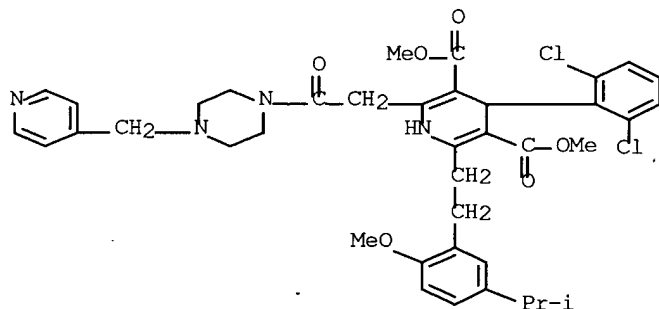


RN 178377-26-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[2-methoxy-5-(1-methylethyl)phenyl]ethyl]-6-[2-oxo-2-[4-(4-pyridinylmethyl)-1-piperazinyl]ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



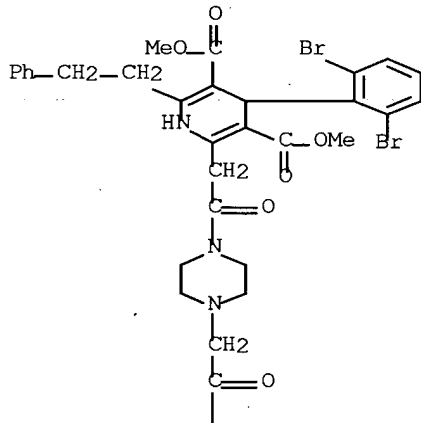
RN 178377-27-0 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[2-methoxy-5-(1-methylethyl)phenyl]ethyl]-6-[2-oxo-2-[4-(4-pyridinylmethyl)-1-piperazinyl]ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 178377-28-1 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dibromophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-piperazinyl]ethyl]-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



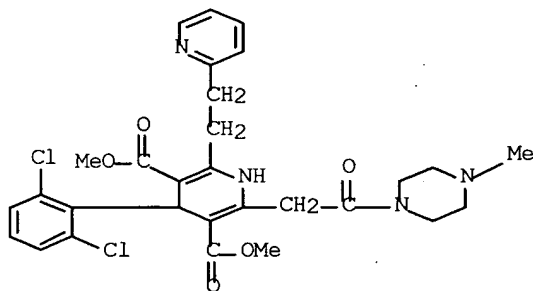
PAGE 2-A



RN 178377-29-2 HCAPLUS

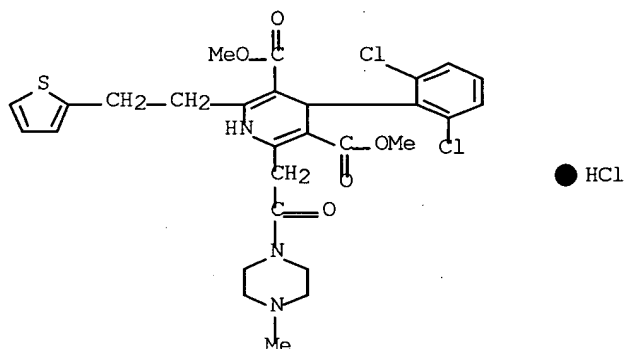
10/813,647

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-[2-(2-pyridinyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



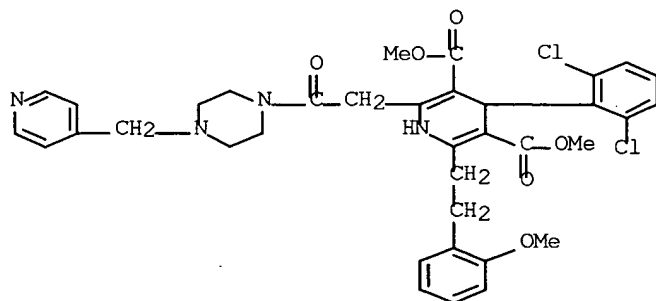
RN 178377-30-5 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-[2-(2-thienyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME).



RN 178377-31-6 HCAPLUS

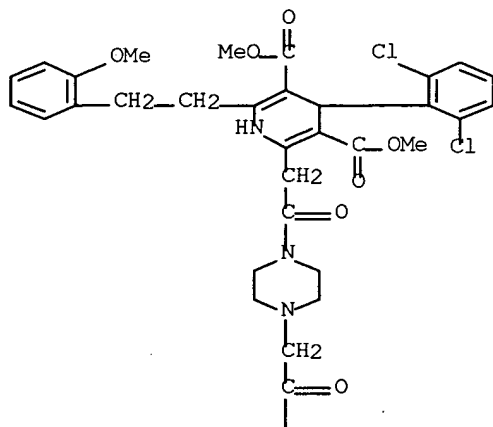
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-(4-pyridinylmethyl)-1-piperazinyl]ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 178377-32-7 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-[2-oxo-2-(1-  
 pyrrolidinyl)ethyl]-1-piperazinyl]ethyl]-, dimethyl ester,  
 monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



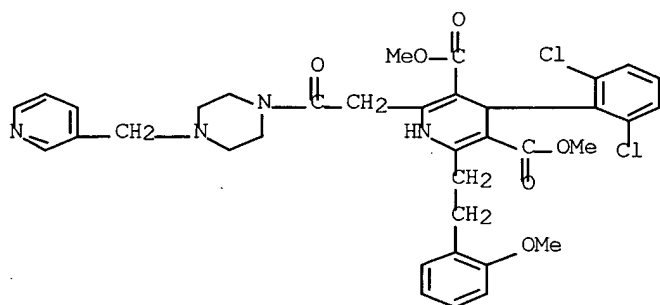
PAGE 2-A



● HCl

RN 178377-33-8 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-  
 2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-(3-pyridinylmethyl)-1-  
 piperazinyl]ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA  
 INDEX NAME)

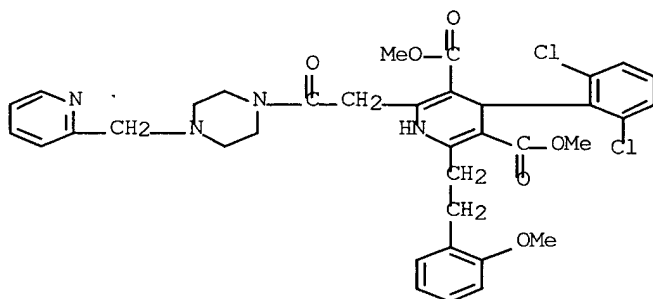
10/813,647



●2 HCl

RN 178377-34-9 HCAPLUS

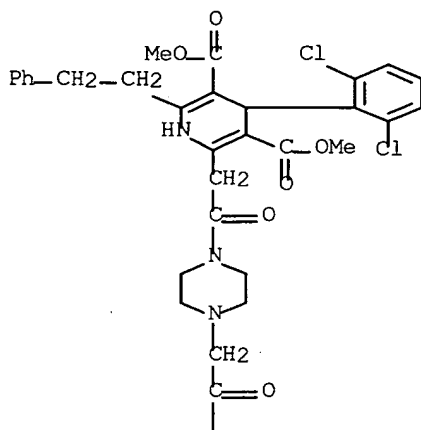
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-(2-pyridinylmethyl)-1-piperazinyl]ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

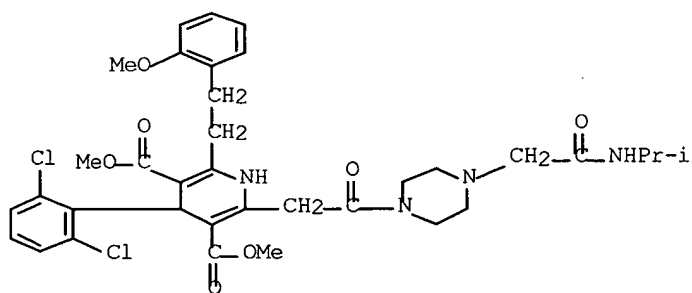
RN 178377-35-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-piperazinyl]ethyl]-6-(2-phenylethyl)-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



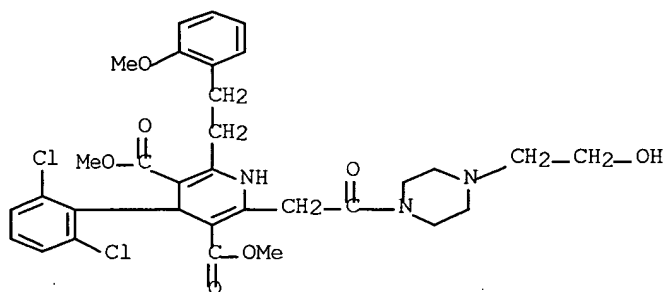
● HCl

RN 178377-36-1 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-[2-[(1-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]-2-oxoethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

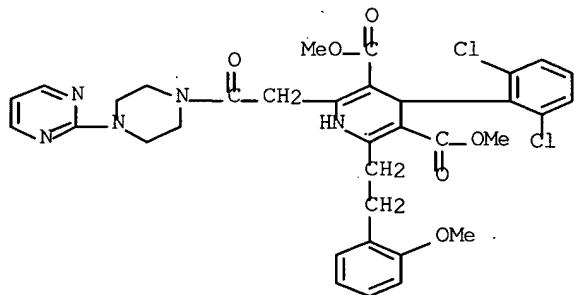
RN 178377-37-2 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(2-hydroxyethyl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

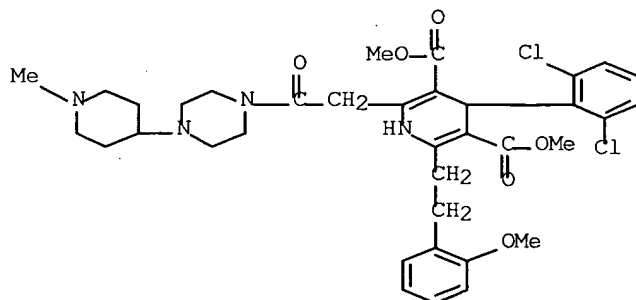
RN 178377-38-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-(2-pyrimidinyl)-1-piperazinyl]ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 178377-39-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(1-methyl-4-piperidinyl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

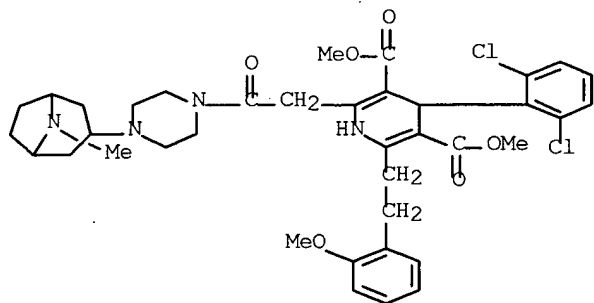


●2 HCl

RN 178377-40-7 HCAPLUS

10/813,647

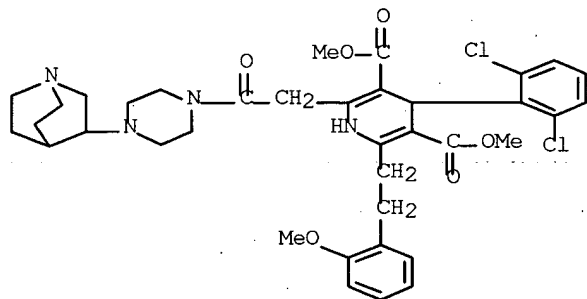
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 178377-41-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(1-azabicyclo[2.2.2]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

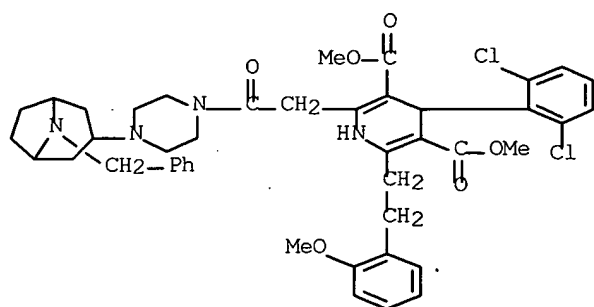


●2 HCl

RN 178377-42-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-[8-(phenylmethyl)-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

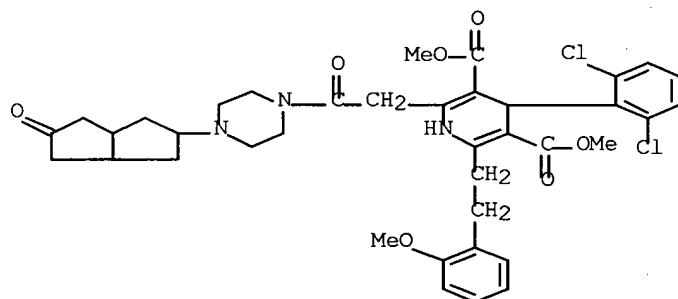




●2 HCl

RN 178377-43-0 HCAPLUS

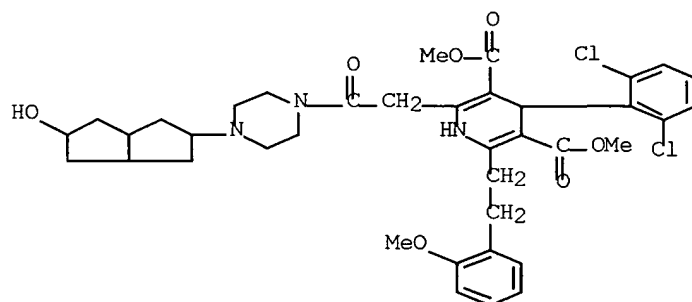
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(octahydro-5-oxo-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 178377-44-1 HCAPLUS

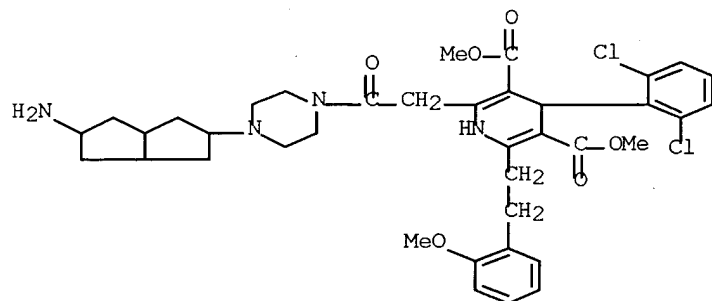
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(octahydro-5-hydroxy-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 178377-45-2 HCAPLUS

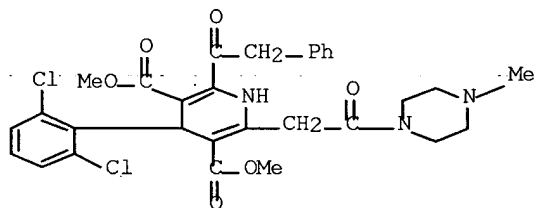
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(5-aminooctahydro-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

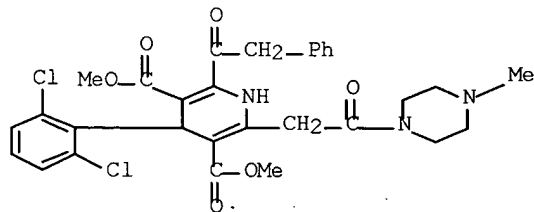
RN 178377-46-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-(phenylacetyl)-, dimethyl ester (9CI) (CA INDEX NAME)



RN 178377-47-4 HCAPLUS

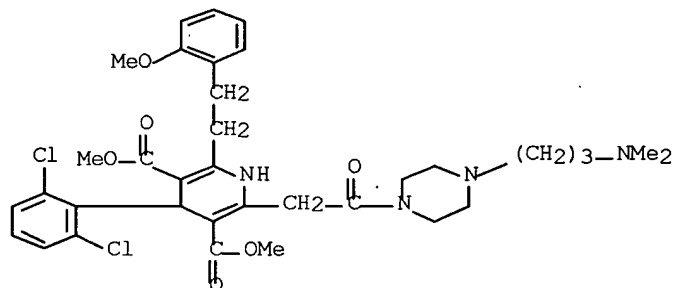
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-(phenylacetyl)-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 178377-48-5 HCAPLUS

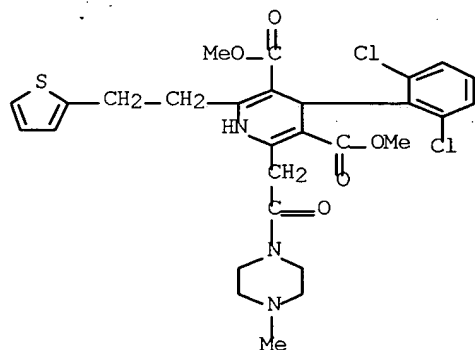
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester, dihydrochloride (9CI)  
(CA INDEX NAME)



●2 HCl

RN 178377-82-7 HCAPLUS

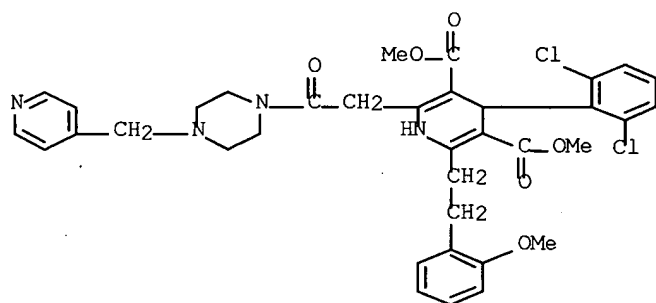
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-6-[2-(2-thienyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 178377-83-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-(4-pyridinylmethyl)-1-piperazinyl]ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

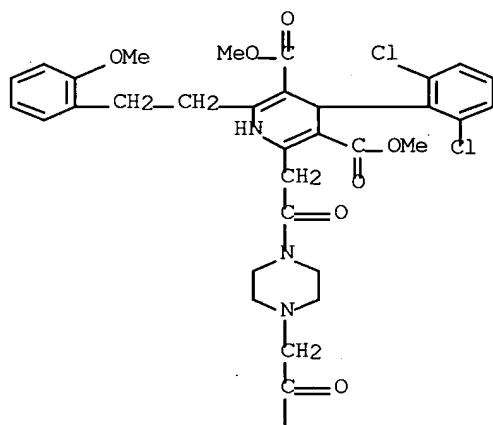
10/813,647



RN 178377-84-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-[2-oxo-2-(1-piperidinyl)ethyl]-1-piperazinyl]ethyl]-, dimethyl ester (9CI)  
(CA INDEX NAME)

PAGE 1-A



PAGE 2-A

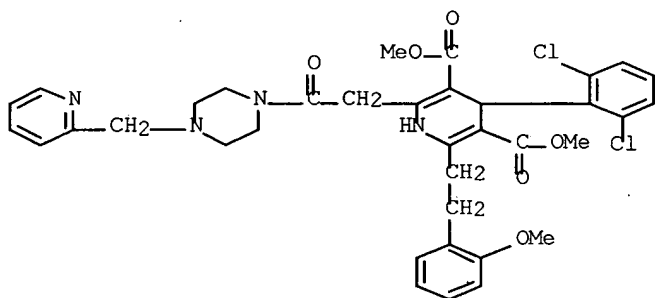


RN 178377-85-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-(3-pyridinylmethyl)-1-piperazinyl]ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

COC(=O)c1cc(CN(C(=O)OCCN2CCCC2Cc3cccnc3)c(=O)OCCN4CCCC4Cc5cccnc5)c(C(=O)OC)c1Cc1ccc(Cl)c(Cl)c1

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-(2-pyridinylmethyl)-1-piperazinyl]ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

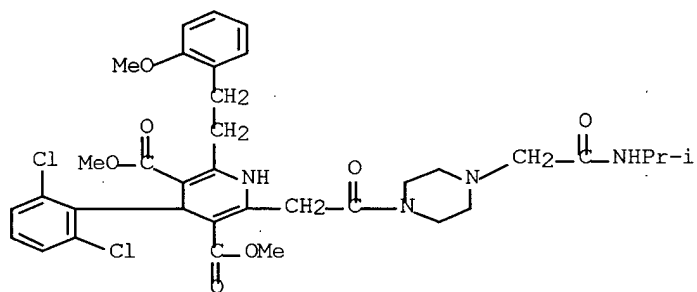


CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-oxo-2-[4-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-piperazinyl]ethyl]-6-(2-phenylethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

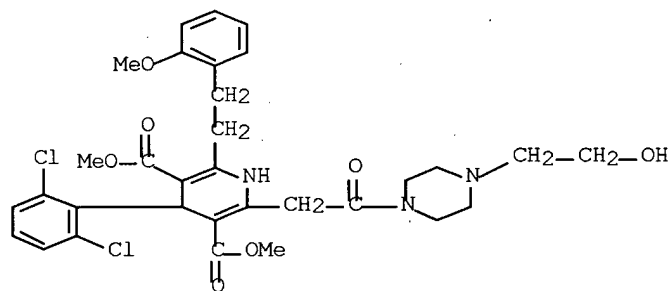
COC(=O)c1c(C(=O)N2CCN(CC2)C(=O)CC3=CC=CC=C3)c(C(=O)OC)c(C(=O)c4cc(Cl)cc(Cl)c4)c1



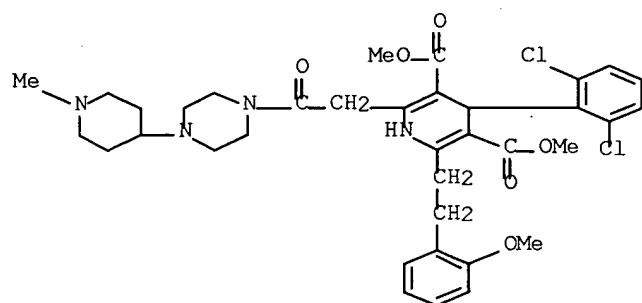
RN 178377-88-3 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-[2-[(1-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]-2-oxoethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 178377-89-4 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-[4-(2-hydroxyethyl)-1-piperazinyl]-2-oxoethyl]-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)

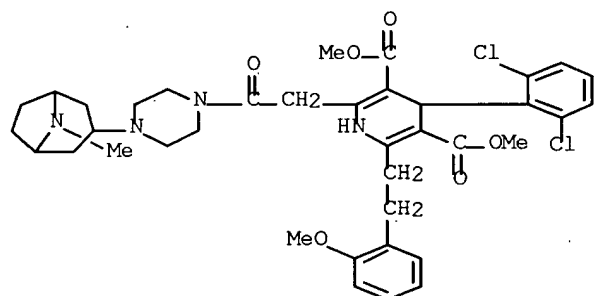


RN 178377-90-7 HCAPLUS  
 CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(1-methyl-4-piperidinyl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



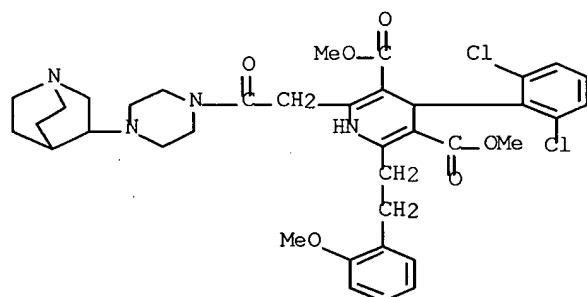
RN 178377-91-8 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



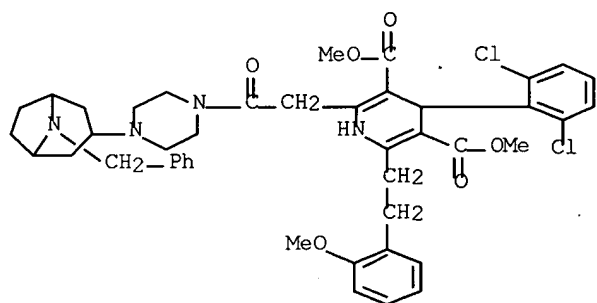
RN 178377-92-9 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(1-azabicyclo[2.2.2]oct-3-yl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



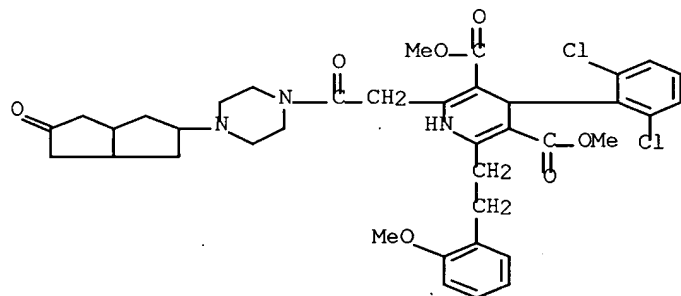
RN 178377-93-0 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-oxo-2-[4-[8-(phenylmethyl)-8-azabicyclo[3.2.1]oct-3-yl]-1-piperazinyl]ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



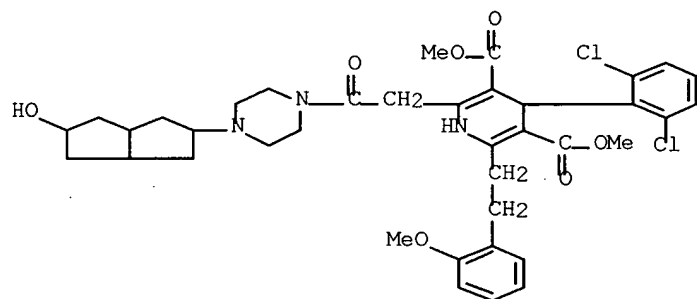
RN 178377-94-1 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(octahydro-5-oxo-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 178377-95-2 HCAPLUS

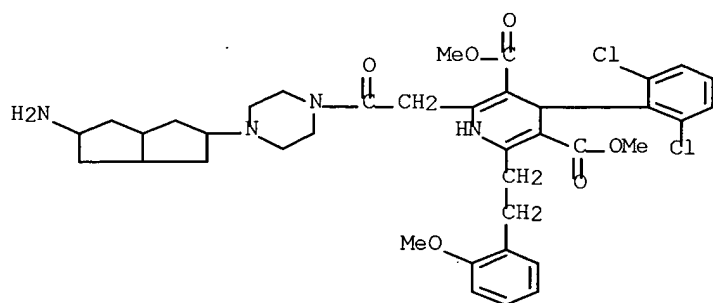
CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-1,4-dihydro-2-[2-(2-methoxyphenyl)ethyl]-6-[2-[4-(octahydro-5-hydroxy-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 178377-96-3 HCAPLUS

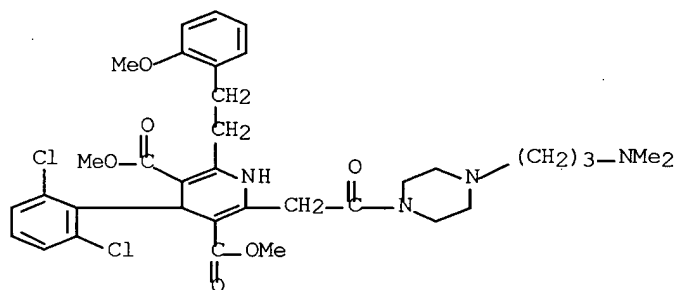
CN 3,5-Pyridinedicarboxylic acid, 2-[2-[4-(5-aminooctahydro-2-pentalenyl)-1-piperazinyl]-2-oxoethyl]-4-(2,6-dichlorophenyl)-1,4-dihydro-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)





RN 178377-97-4 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 4-(2,6-dichlorophenyl)-2-[2-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-2-oxoethyl]-1,4-dihydro-6-[2-(2-methoxyphenyl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



IC ICM C07D211-90

ICS C07D401-12; C07D451-04; C07D401-06; C07D409-06; C07D453-02;  
A61K031-445

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

IT 178376-77-7P 178376-78-8P 178376-79-9P 178376-80-2P  
178376-81-3P 178376-82-4P 178376-83-5P 178376-84-6P  
178376-85-7P 178376-86-8P 178376-87-9P 178376-89-1P  
178376-90-4P 178376-91-5P 178376-92-6P 178376-93-7P  
178376-96-0P 178376-97-1P **178376-98-2P** 178376-99-3P  
178377-00-9P 178377-01-0P 178377-02-1P 178377-03-2P  
178377-04-3P 178377-05-4P 178377-06-5P 178377-07-6P  
178377-08-7P 178377-10-1P 178377-11-2P 178377-13-4P  
178377-14-5P 178377-15-6P 178377-16-7P 178377-17-8P  
178377-18-9P 178377-19-0P 178377-20-3P 178377-21-4P  
178377-22-5P 178377-23-6P 178377-24-7P 178377-25-8P  
**178377-26-9P 178377-27-0P 178377-28-1P**  
**178377-29-2P 178377-30-5P 178377-31-6P**  
**178377-32-7P 178377-33-8P 178377-34-9P**  
**178377-35-0P 178377-36-1P 178377-37-2P**  
**178377-38-3P 178377-39-4P 178377-40-7P**  
**178377-41-8P 178377-42-9P 178377-43-0P**  
**178377-44-1P 178377-45-2P 178377-46-3P**  
**178377-47-4P 178377-48-5P** 178377-63-4P  
178377-78-1P 178377-79-2P 178377-80-5P 178377-81-6P  
**178377-82-7P 178377-83-8P 178377-84-9P**  
**178377-85-0P 178377-86-1P 178377-87-2P**  
**178377-88-3P 178377-89-4P 178377-90-7P**  
**178377-91-8P 178377-92-9P 178377-93-0P**

178377-94-1P 178377-95-2P 178377-96-3P

178377-97-4P 178457-10-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-(piperazinocarbonylmethyl)-1,4-dihydropyridinedicarboxylates as bradykinin antagonists)

L53 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:483690 HCAPLUS Full-text

DOCUMENT NUMBER: 121:83690

TITLE: Syntheses of lobeline analogs with biological activity

AUTHOR(S): Yan, Rian; Zhang, Mingzhe; Shu, Ye

CORPORATE SOURCE: Dep. Chem., Peking Univ., Beijing, Peop. Rep. China

SOURCE: Beijing Daxue Xuebao, Ziran Kexueban (1993), 29(4), 434-9

CODEN: PCTHAP; ISSN: 0479-8023

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Lobelanine, norlobelanine, lobelanidine (I), and norlobelanidine (II) were synthesized. Also obtained were 2,6-diacetonylpiperidine and 2-acetonyl-6-benzoylmethylpiperidine. By the biol. tests on rats, I and II showed good excited effects to the respiratory central system.

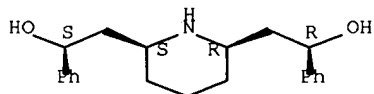
IT 495-49-8P, (±)-Norlobelanidine 552-72-7P, (±)-Lobelanidine 579-21-5P, meso-Lobelanine 6035-31-0P, (±)-Norlobelanine 6168-88-3P 115120-85-9P, (±)-Lobelanidine nitrate 156238-70-9P 156516-42-6P, (±)-Norlobelanidine nitrate

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 495-49-8 HCAPLUS

CN 2,6-Piperidinediethanol,  $\alpha,\alpha'$ -diphenyl-, ( $\alpha R,\alpha'S,2R,6S$ )-rel- (9CI) (CA INDEX NAME)

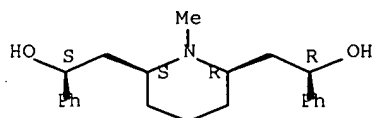
Relative stereochemistry.



RN 552-72-7 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-, ( $\alpha R,\alpha'S,2R,6S$ )-rel- (9CI) (CA INDEX NAME)

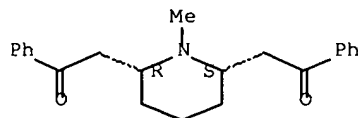
Relative stereochemistry.



RN 579-21-5 HCAPLUS

CN Ethanone, 2,2'-(1-methyl-2,6-piperidinediyl)bis[1-phenyl-, (2R,6S)-rel- (9CI) (CA INDEX NAME)

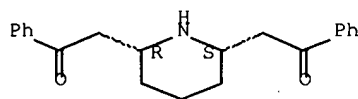
Relative stereochemistry.



RN 6035-31-0 HCAPLUS

CN Ethanone, 2,2'-(2,6-piperidinediyl)bis[1-phenyl-, cis- (9CI) (CA INDEX NAME)

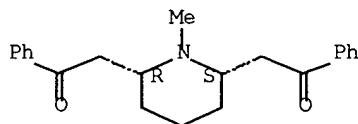
Relative stereochemistry.



RN 6168-88-3 HCAPLUS

CN Ethanone, 2,2'-[(2R,6S)-1-methyl-2,6-piperidinediyl]bis[1-phenyl-, hydrochloride, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

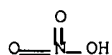
RN 115120-85-9 HCAPLUS

CN 2,6-Piperidinediethanol, 1-methyl- $\alpha,\alpha'$ -diphenyl-, [2 $\alpha$ (R\*),6 $\alpha$ (S\*)]-, nitrate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7697-37-2

CMF H N O3

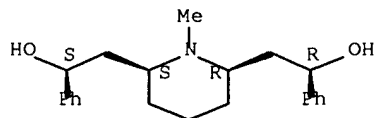


CM 2

CRN 552-72-7

CMF C22 H29 N O2

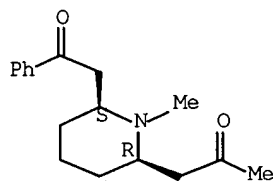
Relative stereochemistry.



RN 156238-70-9 HCAPLUS

CN 2-Propanone, 1-[1-methyl-6-(2-oxo-2-phenylethyl)-2-piperidinyl]-,  
cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



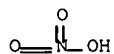
RN 156516-42-6 HCAPLUS

CN 2,6-Piperidinediethanol,  $\alpha,\alpha'$ -diphenyl-,  
[2 $\alpha$ (R\*),6 $\alpha$ (S\*)]-, nitrate (salt) (9CI) (CA INDEX  
NAME)

CM 1

CRN 7697-37-2

CMF H N O3

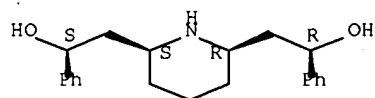


CM 2

CRN 495-49-8

CMF C21 H27 N O2

Relative stereochemistry.



CC 31-3 (Alkaloids)

Section cross-reference(s): 1

ST lobeline alkaloid prepn central nervous .

**system**

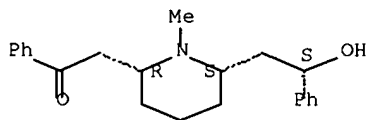
IT 495-49-8P, (±)-Norlobelanidine 552-72-7P,  
 (±)-Lobelanidine 579-21-5P, meso-Lobelanine  
 6035-31-0P, (±)-Norlobelanine 6168-88-3P  
 66120-45-4P 66120-46-5P 108950-19-2P 115120-85-9P,  
 (±)-Lobelanidine nitrate 156238-70-9P 156238-74-3P  
 156516-42-6P, (±)-Norlobelanidine nitrate  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

L53 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1987:208927 HCAPLUS Full-text  
 DOCUMENT NUMBER: 106:208927  
 TITLE: Pupariation in flies: a tool for monitoring  
 effects of drugs, venoms, and other neurotoxic  
 compounds  
 AUTHOR(S): Zdarek, Jan; Fraenkel, Gottfried  
 CORPORATE SOURCE: Inst. Entomol., Czech. Acad. Sci., Prague,  
 Czech.  
 SOURCE: Archives of Insect Biochemistry and Physiology  
 (1987), 4(1), 29-46  
 CODEN: AIBPEA; ISSN: 0739-4462  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A complex Sarcophaga bullata pupariation assay was used to evaluate the neurotropic effects of several drugs, venoms, and insecticides. The assay consists of tests for (1) immediate effects on the intact larva, (2) effects on ligated (i.e., isolated from the **central nervous system**) larval abdomens, (3) morphogenetic effects on the puparium, and (4) effects on stereotyped pupariation behavior. The latter are monitored barog. by recording changes in hemocoelic pressure. Of 62 compds. screened, 18 showed morphogenetic activity at a threshold dose of ≤5 µg, 11 at 50 µg, 4 at 100 µg, and 29 showed no morphogenetic activity. From a comparison of the putative pharmacol. actions of the tested compds. with their morphogenetic effects, certain generalizations can be made. Agents that paralyze neuromuscular systems at the peripheral level (i.e., tetrodotoxin [4368-28-9]) or suppress or modify basic motor patterns centrally (i.e., veratrine sulfate [39412-62-9]) cause retention of larval morphol. characters in the puparium. Compds. that stimulate convulsive contractions of segmental musculature (mostly cholinergic drugs like eserine sulfate [64-47-1], nicotine [54-11-5], and organophosphate insecticides) cause retention of larval segmentation on longitudinally contracted puparia. Five compds. (venom of the scorpion, Leirus quinquestriatus, pyrethrins, protoveratrine A [143-57-7], kainic acid [487-79-6], and quisqualic acid [52809-07-1]) stimulate musculature of the denervated abdomen. Barog. monitoring of changes in pupariation behavior appears to be a most sensitive and informative test. It reveals great differences in the ways in which compds. producing seemingly identical morphogenetic effects affect and modify behavior, thus making pharmacol. classification more accurate.

IT 90-69-7, Lobeline  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (toxicity of, to fly; pupariation as monitor for)  
 RN 90-69-7 HCAPLUS  
 CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidiny]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 4-3 (Toxicology)  
 Section cross-reference(s): 1

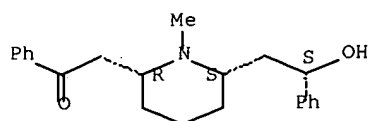
IT 50-55-5, Reserpine 50-67-9, Serotonin, biological studies  
 51-12-7, Nialamide 51-41-2, Norepinephrine 51-43-4 51-67-2,  
 Tyramine 51-83-2 54-11-5, Nicotine 54-92-2, Iproniazid  
 55-48-1, Atropine sulphate 55-92-5, Acetyl- $\beta$ -methylcholine  
 56-12-2, GABA, biological studies 56-69-9, 5-Hydroxy-DL-  
 tryptophan 56-86-0, L-Glutamic acid, biological studies  
 57-24-9, Strychnine 57-94-3, Tubocurarine chloride 58-08-2,  
 Caffeine, biological studies 59-46-1, Procaine 60-13-9,  
 Amphetamine sulphate 60-92-4, CAMP 62-31-7, Dopamine  
 hydrochloride 64-47-1, Eserine sulphate 64-86-8, Colchicine  
 67-52-7, Barbituric acid 71-91-0, Tetraethylammonium bromide  
 73-05-2 76-74-4, Pentobarbital 90-69-7, Lobeline  
 90-81-3, DL-Ephedrine 92-13-7, Pilocarpine 101-31-5  
 107-49-3, TEPP 114-49-8, Scopolamine hydrobromide 116-06-3,  
 Aldicarb 121-75-5, Malathion 124-87-8, Picrotoxin 128-53-0,  
 N-Ethylmaleimide 130-95-0, Quinine 143-57-7, Protoveratrine A  
 306-40-1, Succinylcholine 333-41-5, Diazinon 362-74-3,  
 Dibutyl CAMP 481-39-0, Juglone 487-79-6, Kainic acid  
 497-30-3, L-Ergothioneine 525-66-6 1199-18-4,  
 6-Hydroxydopamine 1563-66-2, Carbofuran 4368-28-9 5989-77-5,  
 Dihydroergotamine tartrate 7683-59-2, DL-Isoproterenol  
 7786-30-3, Magnesium chloride, biological studies 8006-25-5,  
 Ergotoxine 10043-52-4, Calcium chloride, biological studies  
 15662-33-6, Ryanodine 37231-28-0 39412-62-9 52809-07-1,  
 Quisqualic acid  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological  
 study)  
 (toxicity of, to fly, pupariation as monitor for)

L53 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1982:449706 HCAPLUS Full-text  
 DOCUMENT NUMBER: 97:49706  
 TITLE: Comparison of the degree of discriminability  
 of various drugs using the T-maze drug  
 discrimination paradigm  
 AUTHOR(S): Overton, Donald A.  
 CORPORATE SOURCE: Sch. Med., Temple Univ., Philadelphia, PA,  
 19140, USA  
 SOURCE: Psychopharmacology (Berlin, Germany) (  
 1982), 76(4), 385-95  
 CODEN: PSCHDL; ISSN: 0033-3158  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A report of preclin. data that may predict the amount of state-dependent learning  
 likely to be produced in humans by various psychoactive drugs is presented. In a T-  
 maze, rats were required to turn right when drugged and left when not drugged to escape  
 from elec. shock. The number of training sessions required to learn this drug vs. no  
 drug discrimination was used as an indicator of the degree of discriminability of the  
 training drug. Using this procedure, the discriminability of more than 100 common  
 psychoactive drugs was determined at one or more doses. Sessions to criterion usually  
 decreased as dosage was increased. maximum discriminability occurred at the highest  
 usable dose in most cases, and differed considerably for drugs of various types. The  
 results suggest that the majority of psychoactive drugs can be investigated by use of  
 the drug discrimination technique, and that state-dependent learning effects will not  
 accompany clin. use of most psychoactive drugs unless intoxicating doses are used.

IT 90-69-7  
 RL: BIOL (Biological study)  
 (discrimination behavior from)  
 RN 90-69-7 HCAPLUS  
 CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-  
 piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-11 (**Pharmacology**)

IT Analgesics

Anesthetics

Anticonvulsants and Antiepileptics

Antidepressants

Antihistaminics

Antitussives

**Central nervous system** depressants

**Central nervous system** stimulants

Muscle relaxants and Spasmolytics

Narcotics

Neurotransmitter antagonists

Psychotomimetics

Sympatholytics

Sympathomimetics

Opiates and Opioids

RL: BIOL (Biological study)

(discrimination behavior from)

IT 50-06-6, biological studies 50-12-4 50-36-2 50-48-6  
 50-49-7 50-52-2 50-53-3, biological studies 50-55-5  
 50-60-2 50-78-2 51-12-7 51-34-3 51-40-1 51-55-8,  
 biological studies 51-61-6, biological studies 51-64-9  
 51-71-8 51-74-1 51-79-6 51-83-2 52-86-8 52-88-0  
 54-04-6 54-11-5 54-36-4 54-92-2 54-95-5 56-34-8  
 57-27-2, biological studies 57-41-0 57-42-1 57-44-3  
 57-47-6 57-53-4 58-08-2, biological studies 58-25-3  
 58-73-1 59-26-7 59-33-6 59-46-1 59-96-1 59-98-3  
 60-29-7, biological studies 60-40-2 60-41-3 60-80-0  
 63-75-2 64-17-5, biological studies 64-20-0 64-65-3  
 65-29-2 67-64-1, biological studies 67-66-3, biological  
 studies 69-23-8 69-72-7, biological studies 71-82-9  
 72-44-6 76-57-3 76-74-4 76-99-3 77-10-1 77-20-3  
 77-21-4 77-67-8 78-44-4 86-13-5 86-34-0 **90-69-7**  
 92-13-7 103-90-2 110-89-4, biological studies 113-45-1  
 121-75-5 124-87-8 125-64-4 125-71-3 125-72-4 127-48-0  
 129-03-3 129-49-7 132-17-2 137-58-6 141-78-6, biological  
 studies 144-11-6 155-09-9 155-41-9 302-40-9 359-83-1  
 428-37-5 439-14-5 465-65-6 469-62-5 492-41-1 523-87-5  
 525-66-6 532-03-6 546-48-5 561-27-3 604-75-1 919-16-4  
 971-74-4 990-73-8 1002-16-0 1668-19-5 3572-80-3  
 4502-13-0 5714-77-2 5786-21-0 6700-56-7 6740-88-1  
 7439-93-2, biological studies 7491-74-9 7647-01-0, biological  
 studies 7647-14-5, biological studies 7683-59-2 8015-54-1  
 9002-60-2, biological studies 12794-10-4D, derivs. 14838-15-4  
 16590-41-3 17617-23-1

RL: BIOL (Biological study)

(discrimination behavior from)

L53 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:461874 HCAPLUS Full-text

DOCUMENT NUMBER: 93:61874

TITLE: Agonist-induced affinity alterations of a  
**central nervous**

**system**  $\alpha$ -bungarotoxin receptor

AUTHOR(S): Lukas, Ronald J.; Bennett, Edward L.

CORPORATE SOURCE: Lawrence Berkeley Lab., Univ. California,  
 Berkeley, CA, 94720, USA

SOURCE: Journal of Neurochemistry (1979),

33(6), 1151-7

CODEN: JONRA9; ISSN: 0022-3042

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Pretreatment of  $\alpha$ -bungarotoxin (I) [11032-79-4] receptors from rat brain membrane with cholinergic agonist, but not antagonist, caused transformation of sites to a high-affinity form toward agonist. This change in receptor state occurred with a half-time of the order of minutes, and was fully reversible on dilution of agonists, suggesting that I-binding sites are true central nicotinic acetylcholine [51-84-3] receptors. Agonist-induced alteration of receptor state may represent an in vitro correlate of physiol. desensitization. The effects of agonist on I binding isotherms and on the rate of I binding to specific sites suggested that inhibition of I binding to the high-affinity state is noncompetitive. Thus, there may be discrete I-binding and agonist-binding sites on central toxin receptors.

IT 90-69-7

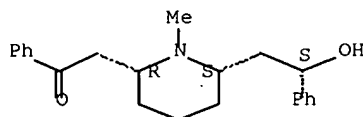
RL: BIOL (Biological study)

(bungarotoxin binding by brain inhibition by)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 2-1 (Hormone **Pharmacology**)

Section cross-reference(s): 1

ST brain bungarotoxin receptor characterization; **central nervous system** bungarotoxin receptor; acetylcholine receptor brain bungarotoxin

IT Receptors

RL: BIOL (Biological study)

(for bungarotoxin, of **central nervous****system**, nicotinic acetylcholine receptors in relation to)

IT 51-83-2 54-11-5 57-94-3 60-26-4 **90-69-7** 153-76-4  
156-74-1 3426-74-2 4468-05-7 4555-00-4

RL: BIOL (Biological study)

(bungarotoxin binding by brain inhibition by)

IT 51-84-3, biological studies

RL: BIOL (Biological study)

(receptors for, bungarotoxin receptors of **central nervous system** in relation to)

IT 11032-79-4

RL: BIOL (Biological study)

(receptors for, of **central nervous****system**, nicotinic acetylcholine receptors in relation to)

L53 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1979:400482 HCAPLUS Full-text

DOCUMENT NUMBER: 91:482

TITLE: Effects of thio-group modification and calcium(2+) ion on agonist-specific state transitions of a central nicotinic acetylcholine receptor

AUTHOR(S): Lukas, Ronald J.; Morimoto, Hiromi; Bennett, Edward L.

CORPORATE SOURCE: Lab. Chem. Biodyn., Univ. California, Berkeley, CA, 94720, USA



SOURCE: Biochemistry (1979), 18(11), 2384-95  
 CODEN: BICHAW; ISSN: 0006-2960  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Agonist-binding affinities of **central nervous system** nicotinic acetylcholine [51-84-3] receptors (nAChR) from rat brain membranes were sensitive to the duration of exposure to agonist. These agonist-induced changes in receptor state were mimicked by appropriate modification of receptor thio-groups (organic disulfide and sulfhydryl residues) and(or) by manipulation of solvent ionic composition. In the absence of  $\text{Ca}^{2+}$ , the concentration of acetylcholine necessary to prevent half of specific  $\alpha$ -bungarotoxin-3H binding was .apprx.1 mM for nAChR treated with dithiothreitol (DTT) or DTT-N-ethylmaleimide (low-affinity states) and .apprx.40  $\mu\text{M}$  for nAChR treated with DTT-dithiobis(2-nitrobenzoic acid) or for native nAChR pretreated with acetylcholine (high-affinity states). Addition of  $\text{Ca}^{2+}$  increased the effectiveness of acetylcholine toward blocking toxin binding. None of these treatments altered toxin or antagonist binding, nor were there observed differences in Hill nos. for agonist binding. Agonists competitively inhibited toxin binding to low-affinity states, but noncompetitive inhibition was observed for binding to high-affinity states. Values of acetylcholine dissociation consts. estimated from these data fell within the range of values determined physiol. with nAChR from other systems. The redox state of brain nAChR thio-groups and  $\text{Ca}^{2+}$  may mediate physiol. important changes in the receptor state during activation and desensitization.

IT 134-63-4

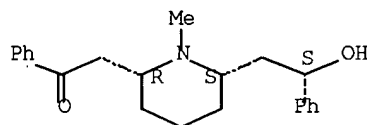
RL: BIOL (Biological study)

(brain binding of, calcium and sulfur-containing group in relation to)

RN 134-63-4 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

CC 2-1 (Hormone Pharmacology)

Section cross-reference(s): 1

IT 51-83-2 51-84-3, biological studies 56-34-8 57-94-3  
 60-25-3 65-29-2 98-04-4 134-63-4 541-22-0  
 1866-16-6 2820-51-1 4468-05-7

RL: BIOL (Biological study)

(brain binding of, calcium and sulfur-containing group in relation to)

L53 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1977:78724 HCAPLUS Full-text

DOCUMENT NUMBER: 86:78724

TITLE: Paper-electrophoretic study of analeptic drugs

AUTHOR(S): Pesakhovich, Ya. L.

CORPORATE SOURCE: Tyumen. Med. Inst., Tyumen, USSR

SOURCE: Farmatsevtichnii Zhurnal (Kiev) (1976)  
 ), (6), 58-60

CODEN: FRZKAP; ISSN: 0367-3057

DOCUMENT TYPE: Journal

LANGUAGE: Ukrainian

AB Paper electrophoresis during 1 h at 400 V and pH 1.8, 2.3, and 3-10 enabled differentiation of nicotinic acid diethylamide [59-26-7], Corazole [54-95-5], cytisine

10/813,647

[485-35-8], lobeline-HCl [ 134-63-4], and strychnine nitrate [66-32-0] concomitantly present on 1 paper.

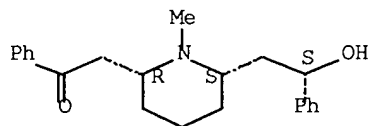
IT 134-63-4

RL: ANT (Analyte); ANST (Analytical study)  
(detection of, by paper electrophoresis)

RN 134-63-4 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidiny]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

CC 64-3 (Pharmaceutical Analysis)

IT Central nervous system stimulants

(detection of, by paper electrophoresis)

IT 54-95-5 59-26-7 66-32-0 134-63-4 485-35-8

RL: ANT (Analyte); ANST (Analytical study)  
(detection of, by paper electrophoresis)

L53 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1973:79794 HCAPLUS Full-text

DOCUMENT NUMBER: 78:79794

TITLE: Nicotine as a discriminative cue in rats.  
Inability of related drugs to produce a  
nicotine-like cuing effect

AUTHOR(S): Schechter, Martin D.; Rosecrans, John A.  
CORPORATE SOURCE: Dep. Pharmacol., Med. Coll. Virginia,  
Richmond, VA, USA

SOURCE: Psychopharmacologia (1972), 27(4),  
379-87

CODEN: PSYPAG; ISSN: 0033-3158

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rats were trained to enter one arm of a T-maze after s.c. injection of nicotine (I) [54-11-5] (0.4mg/kg) and to enter the opposite arm following injection of an equal volume of saline. Nicotine isomethonium iodide-HI (0.4 mg/kg) [38885-20-0], lobeline sulfate [134-64-5] (0.4-10.0mg/kg), d-amphetamine sulfate [51-63-8] (2.0-4.0mg/kg), and arecoline-HBr [300-08-3] (0.25- 2.0mg/kg) produced responses which resembled the established saline effect. Pretreatment with 10.0 mg lobeline/kg did not affect the I-cued response. The cues to which rats respond may be mediated by a central effect of I, while the other drugs may have different effects on the central nervous system.

IT 134-64-5

RL: BIOL (Biological study)  
(behavior in response to, nicotine conditioned response in  
relation to)

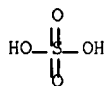
RN 134-64-5 HCAPLUS

CN Ethanone, 2-[(2R)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidiny]-1-phenyl-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-93-9

CMF H2 O4 S

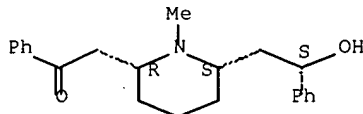


CM 2

CRN 90-69-7

CMF C22 H27 N O2

Absolute stereochemistry.



CC 1-5 (Pharmacodynamics)

IT 51-63-8 134-64-5 300-08-3 38885-20-0

RL: BIOL (Biological study)

(behavior in response to, nicotine conditioned response in relation to)

L53 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1968:94448 HCAPLUS Full-text

DOCUMENT NUMBER: 68:94448

TITLE: Effects of pharmacological agents on the physiological responses of hair disks

AUTHOR(S): Smith, Kenneth Rupert, Jr.; Creech, Brevator J.

CORPORATE SOURCE: Univ. Oxford, Oxford, UK

SOURCE: Experimental Neurology (1967), 19(4), 477-82

CODEN: EXNEAC; ISSN: 0014-4886

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hair disks are specialized pads of epidermis from the dorsal lumbar region of hooded or Sprague-Dawley rats with slowly adapting, highly sensitive touch receptors. Granules in the cytoplasm of the cells are believed to serve as neurotransmitters to initiate generator potentials in the neural membrane. Action potentials elicited from these hair disks by standard mech. stimuli were recorded before and after topical applications of drugs implicated in neurotransmission in the **central** and peripheral **nervous system**. Of the 51 substances tried, only nicotine, lobeline, veratrum alkaloids, K<sup>+</sup>, Ca<sup>2+</sup>, and Mg<sup>2+</sup> blocked the responses of the mechanoreceptor. Nicotine caused stimulation initially. Acetylcholine, serotonin, catechol amines and related drugs had no effect.

IT 90-69-7

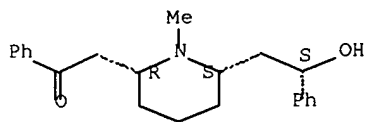
RL: BIOL (Biological study)

(epidermal mechanoreceptor response to)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 15 (**Pharmacodynamics**)  
 IT 54-11-5, biological studies 90-69-7 7439-95-4,  
 biological studies 7440-09-7, biological studies 7440-70-2,  
 biological studies  
 RL: BIOL (Biological study)  
 (epidermal mechanoreceptor response to)

L53 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1965:94011 HCAPLUS Full-text  
 DOCUMENT NUMBER: 62:94011  
 ORIGINAL REFERENCE NO.: 62:16861e-f  
 TITLE: Effect of drugs affecting the **central nervous system** on the total concentration of catechol amine in the blood  
 AUTHOR(S): Unghvary, L.; Hovanyi, M.; Farkas, F.  
 SOURCE: Pharmazeutische Zentralhalle fuer Deutschland (1965), 104(1), 27-9  
 CODEN: PHZEAD; ISSN: 0369-9773

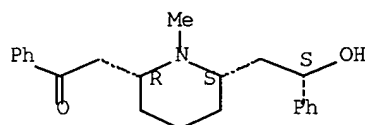
DOCUMENT TYPE: Journal  
 LANGUAGE: German

AB Barbiturates, salicylates, antihistamines, strychnine, amphetamine, scopolamine, pethidine, caffeine, and meprobamate did not show any influence on the catechol amine contents of the blood. However, phenothiazine derivs., acetylcholine, atropine, and Rauwolfia preps. lower the catechol amine level in blood by about 50%, while lobeline-HCl, camphor, pentetrazol, morphine, and EtOH raise it by about 50%. The maximum changes occur after 15-30 min. and return to normal after 60 min.

IT 134-63-4, Lobeline, hydrochloride  
 (effect on pyrocatechol amines in blood)

RN 134-63-4 HCAPLUS  
 CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

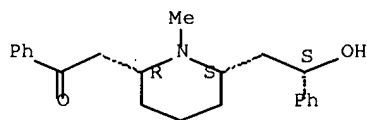
CC 68 (**Pharmacodynamics**)  
 IT 51-84-3, Choline, acetyl- 134-63-4, Lobeline, hydrochloride  
 (effect on pyrocatechol amines in blood)

L53 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1963:5140 HCAPLUS Full-text  
 DOCUMENT NUMBER: 58:5140  
 ORIGINAL REFERENCE NO.: 58:845d-f  
 TITLE: Dimerflin (Rec 7-0267), other **central nervous system** stimulants, and lobeline as antagonists of pentobarbital

AUTHOR(S): Setnikar, Ivo; Murmann, Walter; Magistretti, Maria Jose  
 CORPORATE SOURCE: Recordati S.P.A., Milan  
 SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1962), 138, 364-88  
 CODEN: AIPTAK; ISSN: 0003-9780  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

- AB Various amts. of pentobarbital Na (I) were injected intraperitoneally into mice. Different amts. of stimulants for the **central nervous system** were injected subcutaneously. Compds. which counteracted the lethal effects of I were Rec 7-0267 (2-phenyl-3-methyl-7-methoxy-8-dimethylaminomethylchromone-HCl) (II), Rec 7-0105 (2,3-dimethyl-7-methoxy-8-morpholinomethyl-chromone-HCl), bemegride, pentetrazole, and picrotoxin. Mechanisms of the antagonisms appeared to be functional rather than a competition for receptors. II was the most active. Some compds. did not antagonize the lethal action of I, although I antagonized the lethal effects of the compds. in question. These compds. included vanillic acid diethylamide, 3-ethoxy-4-hydroxybenzoic acid, 5,7-diphenyl-1,3-diazadamantan-6-ol, and d-amphetamine (III). No necessary correlations were found between action against the lethal effects of I and an antihypnotic activity against I. The toxicity of nikethamide and prethcamide was increased by I and these 2 compds. also increased the toxicity of I. The results suggest that in human pharmacotherapy against the action of I and similar barbiturates in toxic doses, brain-stem stimulating compds. would be of value for saving life, but not for awakening the individuals. For the latter purpose, III should be much more effective. 19 references.
- IT 90-69-7, Lobeline  
 (pentobarbital toxicity antagonism by)
- RN 90-69-7 HCAPLUS
- CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- CC 68 (Pharmacodynamics)
- IT 54-95-5, 5H-Tetrazoloazepine, 6,7,8,9-tetrahydro- 90-69-7  
 , Lobeline 1165-48-6, Flavone, 8-[(dimethylamino)methyl]-7-methoxy-3-methyl- 3818-64-2, Chromone, 7-methoxy-2,3-dimethyl-8-(morpholinomethyl)-  
 (pentobarbital toxicity antagonism by)

L53 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1959:73869 HCAPLUS Full-text

DOCUMENT NUMBER: 53:73869

ORIGINAL REFERENCE NO.: 53:13394g-h

TITLE: The action of lobeline and cytotoxone on the cardiovascular system and respiration

AUTHOR(S): Maisaya, V. R.

CORPORATE SOURCE: State Med. Inst., Tiflis

SOURCE: Soobshcheniya Akademii Nauk Gruzinskoi SSR (1958), 21, 365-8

CODEN: SAKNAH; ISSN: 0002-3167

DOCUMENT TYPE: Journal

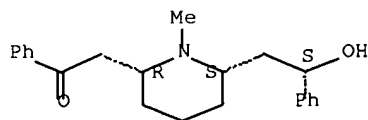
LANGUAGE: Unavailable

- AB In expts. on frogs (*Rana ridibunda*) and cats, cytotoxone (I) and lobeline (II) induce excited breathing and increase in blood pressure not only by stimulation of the carotid sinus, but also by perfusion at the rear extremity, although the latter effect is not quite as strong. Solns. of low concentration were effective (1:80,000-1:10,000 of II, and 1:1,000,000-1:100,000 of I). However, subcutaneous and intramuscular introduction

at even 5-10 times these concns. produced no effect. These drugs are therefore believed to act either directly through the vascular **system**, or through the **central nervous system**.

IT 90-69-7, Lobeline  
(effect on blood pressure and respiration)  
RN 90-69-7 HCAPLUS  
CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 11H (Biological Chemistry: **Pharmacology**)

IT 90-69-7, Lobeline  
(effect on blood pressure and respiration)

L53 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1958:89282 HCAPLUS Full-text

DOCUMENT NUMBER: 52:89282

ORIGINAL REFERENCE NO.: 52:15739g-h

TITLE: The site of action of trans- $\pi$ -oxocamphor, aminocordine, and lobeline by means of circulatory perfusion of head of living dog

AUTHOR(S): Ogawa, Kiichi

CORPORATE SOURCE: Univ. Tokyo

SOURCE: Nippon Yakurigaku Zasshi (1957), 53(Breviaria 25(in English)), 495-507  
CODEN: NYKZAU; ISSN: 0015-5691

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

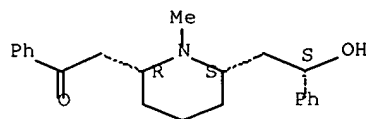
AB Respiratory stimulant effect of these 3 compds. was studied and their sites of action were analyzed by means of crossed head perfusion method in the living dog. The effect of lobeline was shown to be purely reflex in origin, that of trans- $\pi$ -oxocamphor and aminocordine chiefly central. Reflex respiratory stimulation by trans- $\pi$ -oxocamphor and aminocordine when given in the trunk circulation in very large doses was abolished by bilateral vagotomy.

IT 90-69-7, Lobeline  
(respiration stimulation by)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 11H (Biological Chemistry: **Pharmacology**)

IT 59-47-2, 1,2-Propanediol, 3-o-tolyloxy-  
(**nervous system (central)** and)

IT 90-69-7, Lobeline  
(respiration stimulation by)

L53 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1958:2911 HCAPLUS Full-text

DOCUMENT NUMBER: 52:2911

ORIGINAL REFERENCE NO.: 52:584g-h

TITLE: Effects of some drugs on resistance to anemia instigation in the **central nervous system** of frogs

AUTHOR(S): Odintsova, N. V.

CORPORATE SOURCE: S. M. Kirov Med. Inst., Gorki

SOURCE: Farmakologiya i Toksikologiya (Moscow) (1957), 20(No. 4), 54-7

CODEN: FATOAO; ISSN: 0014-8318

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

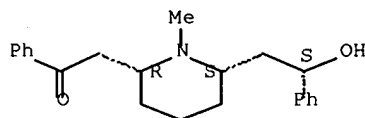
AB Analeptics which favor hematogenesis raise the resistance of the frog **central nervous system** to anemia-producing conditions. In descending order of efficacy, the tested drugs were: adrenalina, atropine, strychnine, lobeline, and caffeine.

IT 90-69-7, Lobeline  
(effect on **central nervous system** in anemia resistance)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 11H (Biological Chemistry: **Pharmacology**)

IT Anemia  
(resistance to, drug effect on **central nervous system** in)

IT 90-69-7, Lobeline  
(effect on **central nervous system** in anemia resistance)

L53 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1956:45868 HCAPLUS Full-text

DOCUMENT NUMBER: 50:45868

ORIGINAL REFERENCE NO.: 50:8888a-e

TITLE: Pharmacology of amino ketones with nicotinic and anti-nicotinic effects. II

AUTHOR(S): Porszasz, J.; Nador, K.; Gibiszer-Porszasz, K.; Wieszt, T.; Padany, R.

CORPORATE SOURCE: Med. Univ., Budapest

SOURCE: Acta Physiologica Academiae Scientiarum Hungaricae (1955), 7, 139-61

CODEN: APACAB; ISSN: 0001-6756

DOCUMENT TYPE: Journal

LANGUAGE: German

AB cf. C.A. 49, 3394i. A survey was made of the nicotinic or antinicotinic effects on blood pressure, on respiration, on the heart, and on the **central nervous system**, of the following compds: 1-piperidino-2-propanone, 4-(1-pyrrolidinyl)-2-butanone 4-piperidino-2-butanone, 5-piperidino-2-pentanone, 1-piperidino-4,4-dimethyl-3-pentanone, 4-piperidino-3-methyl-2-butanone, 3-(piperidinomethyl)-2-octanone, N,N-bis(2-benzoyl-ethyl)methylamine, 1,6-dipiperidino-3,4-hexanedione, trimethyl(3-oxobutyl)aminonium iodide, (2-oxocyclopentylmethyl)diethylamine, 2-(1-pyrrolidinylmethyl)cyclopentanone, 2-(piperidinomethyl)cyclopentanone, 2-(2-methylpiperidinomethyl)cyclopentanone, 2-(4-ethylpiperidinomethyl)cyclopentanone, 2-(cis-2,6-dimethylpiperidinomethyl)cyclopentanone, (2-

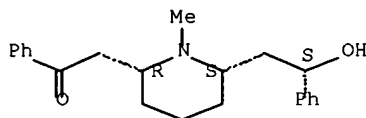
oxocyclohexylmethyl)dimethylamine, (2- oxocyclohexylmethyl)diethylamine, 2-(1-pyrrolidinylmethyl)cyclohexanone, 2-(piperidinomethyl)cyclohexanone, 2-(cis-2,6-dimethylpiperidinomethyl)cyclohexanone, 4-methyl-2-(piperidinomethyl)cyclohexanone, 2-(morpholinomethyl)cyclohexanone, 2-(piperidinomethyl)-1-indanone, 3-(piperidinomethyl)camphor, octahydro-3-(piperidinomethyl)-2(1H)- naphthalenone, 2-(piperidinomethyl)-1-acenaphthenone, N,N-diethylnicotinamide, lobeline, N-benzoyl-ethylmethylamine, 5',6',7',8'-tetrahydro-3-piperidino-2'-propionaphthone, 1-phenyl-5-piperidino-1-penten-3-one, (2- benzoyl-ethyl)trimethylammonium iodide, (2-benzoyl-ethyl)benzyltrimethylammonium bromide, N-(2- benzoyl-ethyl)pyrrolidine; 1-phenyl-5-pyrrolidinyl-1-penten-3-one, N-(2-benzoyl-ethyl)-2-methyl-piperidine, N-(2-benzoyl-ethyl)piperidine, 1-phenyl-4-piperidino-2-butanone, and parpanit.

IT 90-69-7, Lobeline  
(pharmacol. of)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 11H (Biological Chemistry: **Pharmacology**)

IT 59-26-7, Nikethamide 73-63-2, Propiophenone, 3-piperidino-  
90-69-7, Lobeline 94-39-3, Propiophenone,  
3-(1-pyrrolidinyl)- 534-84-9, Cyclohexanone, 2-piperidinomethyl-  
735-81-9, 2'-Propionaphthone, 5',6',7',8'-tetrahydro-3-piperidino-  
1489-51-6, Cyclopentanone, 2-piperidinomethyl- 1489-51-6,  
Piperidine, 1-(2-oxocyclopentylmethyl)- 4756-86-9, 1-Indanone,  
2-piperidinomethyl- 5724-15-2, Ammonium, (2-  
benzoyl-ethyl)trimethyl-, iodide 6784-61-8, 2-Propanone,  
piperidino- 15409-60-6, Cyclohexanone, 2-(dimethylaminomethyl)-  
16635-03-3, 2-Butanone, 4-piperidino- 20177-03-1, 2-Pentanone,  
5-piperidino- 20177-03-1, Piperidine, 1-(4-oxopentyl)-  
24071-91-8, Cyclohexanone, 2-morpholinomethyl- 27152-62-1,  
Propiophenone, 3-methylamino- 31034-98-7, Ammonium,  
trimethyl(3-oxobutyl)-, iodide 33598-33-3, 2-Butanone,  
4-(1-pyrrolidinyl)- 37408-85-8, Cyclohexanone,  
2-(diethylaminomethyl)- 37747-58-3, Piperidine,  
1-(3-camphorylmethyl)- 42327-99-1, 2-Butanone,  
3-methyl-4-piperidino- 42796-37-2, 2-Pipecoline,  
1-(2-benzoyl-ethyl)- 42796-37-2, Propiophenone,  
3-(2-methylpiperidino)- 82087-52-3, Pyrrolidine,  
1-(2-oxocyclohexylmethyl)- 82087-52-3, Cyclohexanone,  
2-(1-pyrrolidinylmethyl)- 82343-79-1, Cyclopentanone,  
2-(diethylaminomethyl)- 90977-79-0, Cyclopentanone,  
2-(1-pyrrolidinylmethyl)- 90977-79-0, Pyrrolidine,  
1-(2-oxocyclopentylmethyl)- 92728-81-9, 2-Butanone,  
1-phenyl-4-piperidino- 101104-66-9, Pyrrolidine,  
1-(2-cinnamoyl-ethyl)- 101104-66-9, 1-Penten-3-one,  
1-phenyl-5-(1-pyrrolidinyl)- 102075-49-0, 1-Penten-3-one,  
1-phenyl-5-piperidino- 102075-49-0, Piperidine,  
1-(3-oxo-5-phenyl-4-pentenyl)- 103756-12-3, Propiophenone,  
3,3'-(methylinino)di- 145208-68-0, 3-Pentanone,  
4,4-dimethyl-1-piperidino- 145208-68-0, Piperidine,  
1-(4,4-dimethyl-3-oxopentyl)- 854884-69-8, Cyclopentanone,  
2-[(4-ethylpiperidino)methyl]- 854884-69-8, Piperidine,  
4-ethyl-1-(2-oxocyclopentylmethyl)- 854905-43-4, Cyclohexanone,  
4-methyl-2-piperidinomethyl- 855372-71-3, Piperidine,  
1-(2-acetylheptyl)- 855372-71-3, 2-Octanone, 3-piperidinomethyl-  
855625-61-5, Camphor, 3-piperidinomethyl- 855911-58-9,

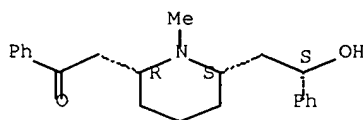


Piperidine, 1,1'-(3,4-dioxohexamethylene)di- 855911-58-9,  
 3,4-Hexanedione, 1,6-dipiperidino- 855946-10-0, Ammonium,  
 (2-benzoyl-ethyl)benzylidimethyl-, bromide 856054-46-1,  
 2(1H)-Naphthalenone, octahydro-3-piperidinomethyl- 856054-46-1,  
 Piperidine, 1-[(decahydro-3-oxo-2-naphthyl)methyl]- 858264-21-8,  
 Cyclopentanone, 2-[(2-methylpiperidino)methyl]- 858264-21-8,  
 Piperidine, 2-methyl-1-(2-oxocyclopentylmethyl)- 858828-39-4,  
 Piperidine, 1-(2-oxo-1-indanylmethyl)- 859297-77-1, Piperidine,  
 1-(2-oxo-1-acenaphthenylmethyl)- 859297-77-1, 1-Acenaphthenone,  
 2-piperidinomethyl- 879552-14-4, Piperidine,  
 2,6-dimethyl-1-(2-oxocyclopentylmethyl)-, cis-  
 (pharmacol. of)

L53 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1955:40405 HCAPLUS Full-text  
 DOCUMENT NUMBER: 49:40405  
 ORIGINAL REFERENCE NO.: 49:7732d-f  
 TITLE: Inhibitors of carbonic anhydrase  
 AUTHOR(S): Keller, Herbert  
 CORPORATE SOURCE: Univ. Bonn a. Rh., Germany  
 SOURCE: Hoppe-Seyler's Zeitschrift fuer Physiologische  
 Chemie (1955), 299, 85-92  
 CODEN: HSZPAZ; ISSN: 0018-4888  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable

AB Sixteen **central nervous system** stimulants were tested for their in vitro effect on carbonic anhydrase. 3-Ethyl-4-cyclohexyl-4H-1,2,4-triazole, metrazole, N, N-diethyl-3,5-dimethyl-4-isoxazolecarboxamide, N,N,N', N'-tetraethylphthalamide, 3-methyl-5-isopropyl-2-cyclohexanone, and nikethamide were inhibitors of this enzyme. Their effect was compared with that of sulfonamides and the theory was proposed that **central nervous system** stimulants exert their effect by blocking gas exchange.  
 IT 90-69-7, Lobeline  
 (carbonic anhydrase inhibition by)  
 RN 90-69-7 HCAPLUS  
 CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 11H (Biological Chemistry: **Pharmacology**)  
 IT 54-95-5, Metrazole 57-24-9, Strychnine 59-26-7, Nikethamide  
 63-74-1, Sulfanilamide 72-14-0, Sulfathiazole 76-22-2, Camphor  
 83-81-8, Phthalamide, N,N,N',N'-tetraethyl- 90-69-7,  
 Lobeline 299-42-3, Ephedrine 329-56-6, Arterenol,  
 hydrochloride 2433-20-7, 4-Isloxazolecarboxamide,  
 N,N-diethyl-3,5-dimethyl- 4671-03-8, 4H-1,2,4-Triazole,  
 4-cyclohexyl-3-ethyl- 7632-10-2, Phenethylamine,  
 N,α-dimethyl- 28587-71-5, Hexetone 855419-09-9, Phenol,  
 p-(1-methyl-1-methylaminoethyl)-, sulfate 860756-42-9, Caffeine,  
 compound with Na salicylate  
 (carbonic anhydrase inhibition by)

L53 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1952:36806 HCAPLUS Full-text  
 DOCUMENT NUMBER: 46:36806  
 ORIGINAL REFERENCE NO.: 46:6270h-i, 6271a  
 TITLE: Influence of various drugs on the action of

curare on the **central nervous system** of the cat  
 AUTHOR(S): Salama, S.; Wright, Samson  
 CORPORATE SOURCE: Middlesex Hosp. Med. School, London  
 SOURCE: British Journal of Pharmacology and Chemotherapy (1952), 7, 14-24  
 CODEN: BJPCAL; ISSN: 0366-0826  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable

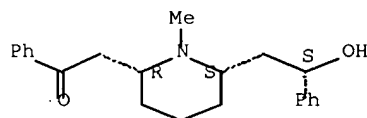
AB cf. preceding abstract Acetylcholine and neostigmine which antagonize strychnine convulsions likewise antagonized curare (I) convulsions. The central inhibitory action of both drugs was partially annulled by atropine. Eserine and hexaethyl tetraphosphate (II), both convulsants, annulled I convulsions; with II the initial inhibition was followed by a secondary stimulation. Me4NI (central depressant), nicotine and lobeline (weak central depressants) annulled I convulsions, nicotine acting only if injected before I. KCl annulled I convulsions when injected intraventricularly, and produced convulsions in normal animals when injected intracisternally.

IT 90-69-7, Lobeline  
 (effect on curare action on **central nervous system**)

RN 90-69-7 HCAPLUS

CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 11H (Biological Chemistry: Pharmacology)

IT Curare  
 (effect on **central nervous system**)

IT 51-84-3, Choline, acetyl- 54-11-5, Nicotine 57-47-6,  
 Physostigmine 75-58-1, Ammonium, tetramethyl-, iodide  
 90-69-7, Lobeline 757-58-4, Ethyl tetraphosphate  
 7447-40-7, Potassium chloride  
 (effect on curare action on **central nervous system**)

L53 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1945:19509 HCAPLUS Full-text

DOCUMENT NUMBER: 39:19509

ORIGINAL REFERENCE NO.: 39:3072i,3073a-b

TITLE: Influence of analeptics on respiration in KCN poisoning

AUTHOR(S): Shvarsalon, N. S.

SOURCE: Farmakologiya i Toksikologiya (Moscow) (1944), 7(No. 3), 29-39

CODEN: FATOAO; ISSN: 0014-8318

DOCUMENT TYPE: Journal

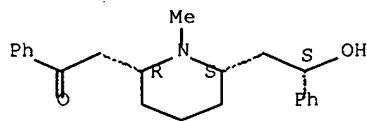
LANGUAGE: Unavailable

AB After intravenous injections of KCN in dogs the use of stimulants for the **central nervous system** during cessation of respiration is contraindicated. In the period of deep, infrequent respiration lobeline and cytitone stimulate respiration, but since they are cardiac depressants their doses must be small. Cytitone (dose 0.1 ml./kg. equivalent to 0.015 mg. cytisine per kg.) is preferable because of lower cardiac activity. Large intravenous doses of adrenaline are beneficial to test animals in KCN poisoning; ephedrine is less effective. Sympatol sometimes stimulates respiration. Like adrenalone, its effect is variable and adrenaline is preferable. Cordiamine and spiramine are ineffective unless the test animal is already in a coma. In the stage of

rapid, shallow breathing respiratory stimulants are superfluous. Respiration charts are shown, and some tests with metrazole are reported.

IT 90-69-7, Lobeline  
(effect on respiration in KCN poisoning)  
RN 90-69-7 HCAPLUS  
CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



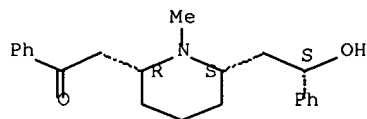
CC 11H (Biological Chemistry: **Pharmacology**)  
IT 51-43-4, Adrenaline 54-95-5, Metrazole 90-69-7,  
Lobeline 299-42-3, Ephedrine  
(effect on respiration in KCN poisoning)

L53 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1932:12172 HCAPLUS Full-text  
DOCUMENT NUMBER: 26:12172  
ORIGINAL REFERENCE NO.: 26:1341i,1342a  
TITLE: The effect of some substances which stimulate  
the **central nervous system** upon respiration and  
circulation  
AUTHOR(S): Gremels, Hans  
SOURCE: Archiv fuer Experimentelle Pathologie und  
Pharmakologie (1931), 162, 29-45  
CODEN: AEXPBL; ISSN: 0365-2041  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable

AB cf. C. A. 25, 346. Cardiazole, coramine, hexetone and lobeline have a therapeutic effect in cardiac insufficiency because of morphine poisoning. They act by stimulating the respiratory center, the depression of which is the chief action of the morphine.

IT 90-69-7, Lobeline  
(effect on cardiac insufficiency due to morphine poisoning)  
RN 90-69-7 HCAPLUS  
CN Ethanone, 2-[(2R,6S)-6-[(2S)-2-hydroxy-2-phenylethyl]-1-methyl-2-piperidinyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 11H (Biological Chemistry: **Pharmacology**)  
IT Circulation  
(effect of substances which stimulate **central nervous system** on)  
IT Respiration  
(of eel, effect of substances which stimulate **central nervous system** on)  
IT **Nervous system**  
(substances stimulating **central**, effect on respiration and circulation)

10/813,647

IT 54-95-5, Metrazole 90-69-7, Lobeline 28587-71-5,  
Hexetone  
(effect on cardiac insufficiency due to morphine poisoning)

=>